

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Patent Application of:

Inventors: Hartung.
Serial No: 10/674,279
Filed: September 29, 2003
Title: PACEMAKER FOR ATRIAL SENSING, ATRIAL
STIMULATION AND TERMINATION OF ATRIAL
TACHYCARDIAS AND AURICULAR FIBRILLATION, AND
A METHOD OF CONTROLLING A CARDIAC PACEMAKER
Assignee: Biotronik Mess- und Therapiegeraete GmbH & Co. Ingenieurbuero
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Berlin, GERMANY D-12359
Art Unit: 3762
Examiner: Alter, Alyssa Margo

APPEAL BRIEF

To: Mail Stop Appeal Brief- Patents
The Honorable Commissioner of Patents and Trademarks
P.O. Box 1450
Alexandria, VA 22313-1450

In response to the Examiner's Office Action of March 5, 2009, made 'Final' of the at least twice rejected claims 1-3, 6, 7, 11, 17, 18, 21, 22, 25 and 27 in the above-identified patent application and the Advisory action of July 17, 2009.

The Applicant's Brief on Appeal is filed within the balance of the two-month time period running from the receipt of the notice of appeal and, therefore, no extension of time is required.

The Applicant's Brief on Appeal is filed with the requisite filing fee under 37 C.F.R. § 41.20(b) (2) of \$540.00. Please charge Deposit Account 15-0450 for any and all fees due for this paper.

This brief contains these items under the following headings and in the order set forth below (37 C.F.R. § 41.37):

- I. Real Party in Interest
- II. Related Appeals and Interferences
- III. Status of Claims
- IV. Status of Amendments
- V. Summary of the Claimed Subject Matter
- VI. Grounds of Rejection to be Reviewed on Appeal
- VII. Arguments
- VIII. Claims Appendix
- IX. Evidence Appendix
- X. Related Proceedings Appendix

The final page of this brief bears the practitioner's signature.

I. Real Party in Interest

The real party in interest in the present application is Biotronik Mess- und Therapiegeraete GmbH & Co. Ingenieurbuero Berlin Woermannkehre 1 Berlin, GERMANY D-12359, by assignment from inventor Dr. Wolfgang Hartung on June 22, 2004. The assignment is recorded in the United States Patent and Trademark Office at Reel 015550, Frame 0450.

II. Related Appeals and Interferences

There have been no interferences relating to this pending application, nor any related appeal or litigation.

III. Status of Claims

The status of the claims in this application is:

1. **Total Number of Claims in Application**

Claims 1-3, 6, 7, 11, 17, 18, 21, 22, 25 and 27 are pending in the application, being a total of 12 claims. Claims 8-10, 12-16, 19-20, 23-24, and 26 are cancelled. No claims are allowed. Claims 1-3, 6, 7, 11, 17, 18, 21, 22, 25 and 27 are rejected and now under appeal.

2. **Status of All of the Claims**

- A. Claims cancelled: 8-10, 12-16, 19-20, 23-24, and 26.
- B. Claims withdrawn from consideration but not cancelled: None.
- C. Claims pending: 1-3, 6, 7, 11, 17, 18, 21, 22, 25 and 27.
- D. Claims allowed: None.
- E. Claims objected to: None.
- F. Claims rejected: 1-3, 6, 7, 11, 17, 18, 21, 22, 25 and 27.

3. **Claims on Appeal**

The claims on appeal are claims 1-3, 6, 7, 11, 17, 18, 21, 22, 25 and 27.

IV. **Status of Amendments**

The claims were last amended on November 21, 2008 at the time of filing of an Amendment in response to Examiner's Office Action of August 25, 2008 in this matter. A response to the Final Office action of March 5, 2009 was filed on May 5, 2009, however, no amendments were made in that response.

No amendments have been filed, subsequent to the rejection from which this appeal was originally taken, contained in the Final Office Action mailed March 5, 2009. A notice of appeal was filed September 1, 2009.

V. Summary of the Claimed Subject Matter

All citations to the specification refer to the substitute specification filed on July 1, 2004. As claimed in independent claim 1, the present invention relates to a cardiac pacemaker arrangement (Fig. 4, paragraphs [0032] & [0033]). The cardiac pacemaker arrangement (Fig. 4) includes at least one floating atrial electrode line (Fig. 4, paragraphs [0032] & [0033] and paragraphs [0045] to [0048]) having an atrial wall electrode (Fig. 4, paragraphs [0032] & [0033] and paragraphs [0045] to [0048]). The cardiac pacemaker further includes a ventricular electrode line (VDD-electrode line) (Fig. 4, paragraphs [0032] & [0033] and paragraphs [0045] to [0048]) having at least one floating atrial electrode (Fig. 4) for stimulation, and at least one ventricular electrode (Fig. 4). The cardiac pacemaker also includes at least one circuit (paragraph [0006], Abstract) adapted to evaluate atrial signals perceived by the electrodes (Fig. 1), and switch over from a first mode, for effecting atrial myocardium stimulation by the atrial wall electrode (Fig. 4), to a second mode, for effecting atrial myocardium stimulation by the at least one floating atrial electrode (Fig. 4), upon perceiving atrial signals that are evaluated as being high-frequency irregularities such as auricular fibrillation or atrial tachycardias as on the basis of inadmissibly high signal frequencies (Fig. 4, paragraphs [0032] & [0033] and paragraphs [0045] to [0048]).

VI. Grounds of Rejection to be Reviewed on Appeal

The current grounds of rejection are from the Final Office Action of March 5, 2009.

The Examiner rejected claims 3, 11, and 27 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. In the rejection, the Examiner states that, with regard to claims 3 and 11, the specification does not provide support for “two or more floating atrial electrodes and two or more ventricular electrodes of said ventricular electrode line”. As to claim 27, the Examiner states that the specification does not provide support for the “atrial wall electrode” and the “floating atrial electrode” being “about the same physical size”.

The Examiner rejected claims 1-3, 6-7, 11, 17-18, 21-22, 25, and 27 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner states that it is unclear

what the Applicant considers to be the “floating atrial electrode line”. Additionally, it is unclear if the “at least one floating atrial electrode line” also possesses a floating atrial electrode in addition to the wall electrode.

The Examiner rejected claims 1-3, 6-7, 11, 17-18, 21-22, 25, and 27 under 35 U.S.C. 103(a) as being unpatentable over Alt et al. (US 6,370,427 B1), hereinafter Alt. In the rejection, the Examiner states that Alt discloses a pacing and defibrillation system. As seen in figure 4 the system includes an electrode line or lead 63 in the atrium with a wall electrode 64 and a floating electrode 62. Electrode 64, or the wall electrode, is used for sensing and pacing the cardiac activity of the atrium. Electrode 62, or the floating electrode, is used to provide a defibrillation shock to the heart. The wall electrode operates in a first mode by sensing and pacing the atrium of the heart, while the floating electrode operates in a second mode to provide defibrillation stimulation. Additionally, figure 4 depicts a ventricular electrode line (VDD-electrode line) as lead 66. The lead also possesses a floating electrode 70. The Examiner further states that Alt discloses the device substantially as claimed except for placing a floating atrial electrode on the ventricular electrode line (VDD-electrode line). It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the electrode lines and electrode placement to include a floating atrial electrode on the same line as a ventricular electrode since it has been held that forming in one piece an article which has formerly been formed in two pieces and put together involves only routine skill in the art. Furthermore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the lead electrodes since it was known in the art that such a modification to place multiple electrodes on one lead would provide the predictable results of reducing the quantity of invasive leads placed into the heart.

VII. Argument

Grouping of Claims

The claims under appeal include independent claim 1, and dependent claims 2-3, 6-7, 11, 17-18, 21-22, 25, and 27. The claims rise or fall together.

Legal Basis for Argument

The statutory standard under 35 U.S.C. §112, first paragraph, is that the specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The Examiner is required to establish a *prima facie* case by providing reasons why a person of ordinary skill in the art would not have recognized that the inventor was in possession of the invention as claimed in view of the disclosure of the application as filed. (MPEP §§ 2163, 2163.04)

It must be pointed out that there is no *in haec verba* requirement regarding compliance with the written description requirement. (MPEP §§ 2163 I.B., 2163.02) Possession of the claimed invention may be shown “by disclosure of drawings ...that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole” (MPEP § 2163 II.A.3.(a)) or “by describing the claimed invention with all its limitations using such descriptive means as words, structures, figures, diagrams and formulas that fully set forth the claimed invention.” (MPEP §§ 2163.02) Also, a description that discloses “a device that inherently performs a function or has a property ... necessarily discloses that function theory or advantage...” (MPEP §§ 2163.07(a))

The statutory standard under 35 U.S.C. §112, second paragraph, is that the specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The statutory standard under 35 U.S.C. §103(a) is that a patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

A claimed invention is unpatentable under 35 U.S.C. §103 if the differences between it and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. 35 U.S.C. § 103 (1994); *Graham v. John Deere Co.*, 383 U.S. 1, 14 (1966). The ultimate determination of whether an invention is or is not obvious is a legal conclusion based on underlying factual inquiries, including (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed invention and the prior art; and (4) objective evidence of nonobviousness. *Graham*, 383 U.S. at 17-18.

The Supreme Court has issued its opinion in *KSR*, regarding the issue of obviousness under 35 U.S.C. §103(a) when the claim recites a combination of elements of the prior art. *KSR Int'l Co. v. Teleflex, Inc.*, No 04-1350 (U.S. Apr. 30, 2007). The Court reaffirmed the *Graham* factors in the determination of obviousness under 35 U.S.C. §103(a). The four factual inquiries under *Graham* are:

- (a) determining the scope and contents of the prior art;
- (b) ascertaining the differences between the prior art and the claims in issue;
- (c) resolving the level of ordinary skill in the pertinent art; and
- (d) evaluating evidence of secondary consideration.

Graham v. John Deere, 383 U.S. 1, 17-18, 148 USPQ 459, 467 (1966).

The Court did not totally reject the use of “teaching, suggestion, or motivation” as a factor in the obviousness analysis. Rather, the Court recognized that a showing of “teaching, suggestion, or motivation” to combine the prior art to meet the claimed subject matter could provide a helpful insight in determining whether the claimed subject matter is obvious under 35 U.S.C. §103(a).

The Court rejected a rigid application of the “teaching, suggestion, or motivation” (TSM) test, which required a showing of some teaching, suggestion, or motivation in the prior art that would lead one of ordinary skill in the art to combine the prior art elements in the manner claimed in the application or patent before holding the claimed subject matter to be obvious.

The Court noted that **the analysis supporting a rejection under 35 U.S.C. §103(a) should be made explicit, and that it was “important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the [prior art] elements” in the manner claimed.**

The Court specifically stated:

Often, it will be necessary...to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an **apparent reason** to combine the known elements in the fashion claimed by the patent at issue. To facilitate review, this analysis **should be made explicit**.

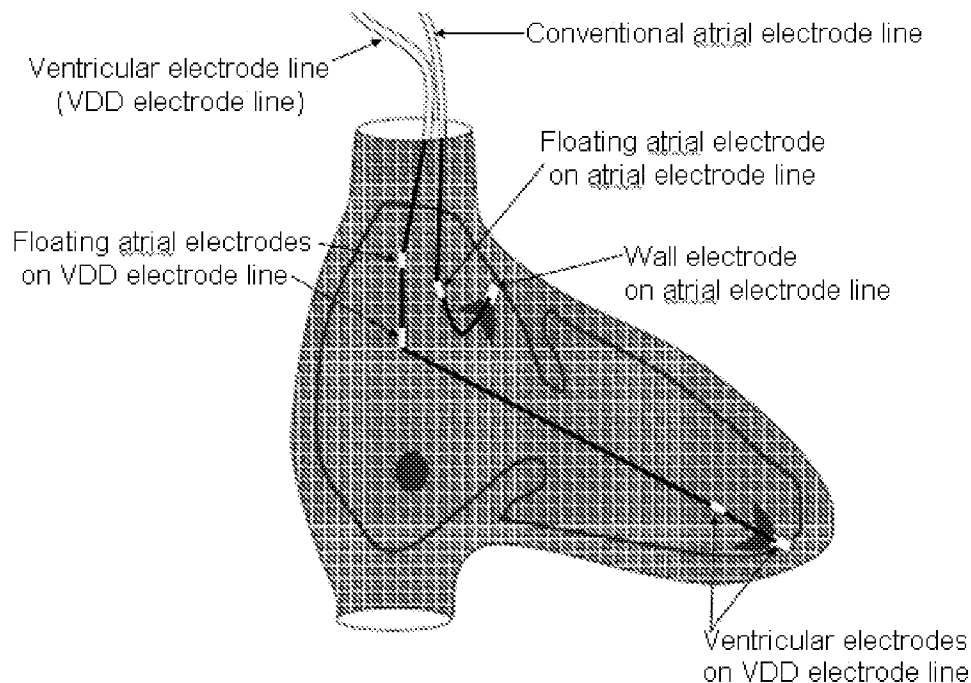
KSR, slip op. at 14 (emphasis added).

Therefore, in formulating a rejection under 35 U.S.C. §103(a) based upon a combination of prior art elements, it remains necessary to identify the reason why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed.

Rejection under 35 U.S.C. 103(a) as being unpatentable over Alt et al. (U.S. Patent No. 6,370,427 B1).

Claims 1-3, 6-7, 11, 17-18, 21-22, 25, and 27

The figure below shows a portion of Fig. 4 of the present application and clearly indicates the conventional atrial electrode line and its associated electrodes, and the ventricular electrode line (VDD electrode line) and its associated electrodes.



The figure shows four (4) electrodes in the atrium of the heart and two electrodes in the ventricle of the heart. Two of the electrodes in the atrium are floating electrodes and are part of the ventricular (VDD) electrode line. The two electrodes in the ventricle are also part of the ventricular (VDD) electrode line toward a distal end thereof. Another electrode in the atrium is a floating electrode and is part of the atrial electrode line. Still another electrode in the atrium is a wall electrode and is also part of the atrial electrode line. The claimed invention of independent claim 1 of the present application requires at least one floating atrial electrode line having an atrial wall electrode and a ventricular electrode line (VDD-electrode line) having at

least one floating atrial electrode for stimulation (emphasis added) and at least one ventricular electrode. The configuration of the figure above shows such electrode lines having the electrodes as claimed by independent claim 1 of the present application. A focus of the arguments herein is the fact that the ventricular electrode line has a floating stimulation electrode located in the atrium. Another focus of the arguments herein is the fact that, in accordance with independent claim 1, the configuration may switch over from a first mode, for effecting atrial myocardium stimulation by an atrial wall electrode of the atrial electrode line, to a second mode, for effecting atrial myocardium stimulation by a floating atrial electrode of the ventricular electrode line.

It is respectfully submitted that Alt does not teach, suggest, or render obvious the claimed invention of independent claim 1. The Examiner argues that providing a floating atrial electrode on a ventricular lead would be obvious because Alt shows an electrode arrangement with a particular atrial electrode lead. However, Applicant disagrees with the Examiner on this point because a floating atrial electrode on a ventricular electrode lead does not replace the atrial electrodes on the atrial electrode lead. Instead, in the claimed invention of claim 1, the floating atrial electrode on the ventricular electrode lead is provided in addition to the atrial electrodes on the atrial electrode lead and that it would not be obvious to do so. Claim 1 expressly states that the arrangement comprises at least one floating atrial electrode line having an atrial wall electrode and, in addition, a ventricular electrode line providing a floating atrial electrode. Providing both an atrial electrode line and a ventricular electrode line that features an additional atrial electrode is contrary to the Examiner's argument and, therefore, should be considered non-obvious.

Furthermore, Alt does not teach or suggest the configuration of Fig. 4 of the present application. The ventricular electrode line (VDD-electrode line) of claim 1 has a floating atrial electrode and a ventricular electrode. The electrode configuration of claim 1 is disclosed in Fig. 4 of the present application and in the description referring to Fig. 4 in paragraph [0032] and [0033] of the present application. With respect to the Examiner's rejection, Alt only discloses a ventricular electrode line that has one electrode in the ventricle. The present application's electrode configuration is neither disclosed nor suggested by Alt.

The claimed arrangement of claim 1 comprises two electrode lines, an atrial electrode line including an atrial wall electrode and a ventricular electrode line including a floating atrial electrode. In a normal (first) mode, atrial stimulation is performed via the atrial wall electrode of the atrial electrode line. In the case of atrial signals indicating high-frequency irregularities, atrial stimulation (not atrial defibrillation) is performed via the floating atrial electrode on the ventricular electrode line. Such an arrangement is neither known from Alt nor made obvious by Alt, since Alt does not show a ventricular electrode line providing a floating atrial electrode. (emphasis added), and Alt does not teach or suggest the situation where, in the case of atrial signals indicating high-frequency irregularities, atrial stimulation (not atrial defibrillation) is performed via the floating atrial electrode on the ventricular electrode line.

Furthermore, the electrode as shown in Alt is a defibrillation electrode and not a stimulation electrode. It is common in the art to refer to stimulation electrodes and defibrillation electrodes which serve different purposes and, therefore, are not the same. The drawings of the present application (particularly Fig. 4) do not show any large surface (coil) electrode that would be used for defibrillation but, instead, show only small surface stimulation electrodes that are of approximately the same size. With respect to the difference between defibrillation electrodes (shock coils) and stimulation electrodes (pacing electrodes), please see Exhibit D of the Evidence Appendix herein. Exhibit D explicitly states that pacing electrodes have a surface area of little more than 1 mm^2 whereas defibrillation electrodes usually have a surface area of more than 500 mm^2 . Please refer to at least the 11th, 12th, and 14th pages of Exhibit D. There can be no doubt that a defibrillation electrode (shock coil) like electrode 62 from figures 3 and 4 of Alt are not stimulation electrodes (pacing electrodes) as the Examiner seems to suggest in the Advisory Action. Furthermore, in the Advisory Action, the Examiner expresses some doubts that the wall electrode and the floating electrode are approximately of the same size. This can be seen from Fig. 4 of the present application, but is even clearer for the man skilled in the art that stimulation (pacing) electrodes have a size of approximately 1 mm^2 and, therefore, are approximately of the same size, as further evidenced by Exhibit D.

Therefore, it would not be obvious to one skilled in the art, having the knowledge disclosed in Alt, to arrive at the cardiac pacemaker arrangement of independent claim 1 of the present application. Especially, it would not be obvious to place a floating atrial electrode on a

ventricular electrode line for the purpose of switching over from a first mode, for effecting atrial myocardium stimulation by an atrial wall electrode of a conventional atrial electrode line, to a second mode, for effecting atrial myocardium stimulation by at least one floating atrial electrode of a ventricular electrode line.

Therefore, the differences between the claimed invention and the prior art are NOT such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art, as required by the test for obviousness under 35 U.S.C. 103(a).

Therefore, in view of at least the foregoing, it is respectfully submitted that independent claim 1 is not rendered obvious by Alt, and it is respectfully submitted that claim 1 defines allowable subject matter. Also, since claims 2-3, 6-7, 11, 17-18, 21-22, 25, and 27 depend either directly or indirectly from independent claim 1, and since Applicant respectfully submits that independent claim 1 is not obvious over Alt, as argued above herein, it is respectfully submitted that claims 2-3, 6-7, 11, 17-18, 21-22, 25, and 27 are allowable as well.

Rejection under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Claims 3, 11, and 27

With respect to claims 3 and 11, Fig. 4 of the present application shows two or more floating atrial electrodes, in particular, two floating atrial electrodes on the ventricular electrode line and one floating atrial electrode on the atrial electrode line. Furthermore, in the present application, the plural term “electrodes” is used throughout and the phrase “two or more electrodes” is clearly encompassed by the plural term “electrodes”. Also, paragraph [0044] of the present application states, “The electrodes that can be used are unipolar and/or bipolar electrodes so that in the present text in part the term “electrode” and in part the term “electrodes” are used, without in that respect in each case meaning exclusively the use of only one or only two or more electrodes.” (emphasis added) With respect to claim 27, it has been clearly discussed herein above why the atrial wall electrode and the floating atrial electrodes would be about the same physical size since they are both stimulation electrodes. Fig. 4 of the present

application clearly indicates this, and Exhibit D clearly supports the contention that stimulation (pacing) electrodes have a size of approximately 1 mm² and, therefore, are approximately of the same size.

Therefore, the claimed invention could easily comply with the written description requirement under 35 U.S.C. 112, first paragraph, with minor adjustments to claims 3 and 11.

Therefore, in view of at least the foregoing, it is respectfully submitted that claims 3, 11, and 27 fully comply with 35 U.S.C. 112, first paragraph, and it is respectfully submitted that claims 3, 11, and 27 define allowable subject matter.

Rejection under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-3, 6-7, 11, 17-18, 21-22, 25, and 27

From the discussion above with respect to the 35 U.S.C. 103(a) rejection, it is clear what constitutes the floating atrial electrode line. It is the atrial electrode line, as shown in Fig. 4 of the present application and in the figure above herein, having an atrial wall electrode and a floating atrial electrode. That is, the term “floating” in “floating atrial electrode line” is intended to indicate that the atrial electrode line includes a floating atrial electrode. However, Applicant may be open to amending claim 1 to more explicitly state that a floating atrial electrode is part of the floating atrial electrode line.

Therefore, the claimed invention does not fail to particularly point out and distinctly claim the subject matter which applicant regards as the invention as required by 35 U.S.C. 112, second paragraph.

Therefore, in view of at least the foregoing, it is respectfully submitted that independent claim 1 complies with 35 U.S.C., second paragraph, and it is respectfully submitted that claim 1 defines allowable subject matter. Also, since claims 2-3, 6-7, 11, 17-18, 21-22, 25, and 27 depend either directly or indirectly from independent claim 1, and since Applicants respectfully

submit that independent claim 1 does not fail to particularly point out and distinctly claim the subject matter which applicant regards as the invention, as argued above herein, it is respectfully submitted that claims 2-3, 6-7, 11, 17-18, 21-22, 25, and 27 are allowable as well.

Conclusion

Applicants respectfully submit that none of claims 1-3, 6-7, 11, 17-18, 21-22, 25, and 27 are rendered obvious by Alt. The Examiner's reasons for such rejections, as outlined in the section herein "Grounds of Rejection to be Reviewed on Appeal", have been refuted herein. Furthermore, Applicants respectfully submit the specification of the present application meets the written description requirement with respect to at least claims 3, 11, and 27, and that the claims do particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to independent claim 1, the operational configuration of Alt is clearly quite different than that of claim 1 of the present application with respect to having a floating atrial electrode on a ventricular electrode lead for the purpose of switching over from a first mode, for effecting atrial myocardium stimulation by an atrial wall electrode of a conventional atrial electrode line, to a second mode, for effecting atrial myocardium stimulation by at least one floating atrial electrode of a ventricular electrode line, as described herein. The limitations of claim 1 of the present application are not taught or suggested by Alt, and certainly would not be obvious to one skilled in the art in light of Alt.

Withdrawal of the rejection of the claims under 35 U.S.C. § 112, first paragraph, 35 U.S.C. § 112, second paragraph, and 35 U.S.C. 103(a), and the issuance of a Notice of Allowance is respectfully requested.

Respectfully submitted,



Date: October 5, 2009

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VIII. Claims Appendix

1. A cardiac pacemaker arrangement comprising:
 - at least one floating atrial electrode line having an atrial wall electrode;
 - a ventricular electrode line (VDD-electrode line) having at least one floating atrial electrode for stimulation, and at least one ventricular electrode; and
 - at least one circuit adapted to:
 - evaluate atrial signals perceived by said electrodes, and
 - switch over from a first mode, for effecting atrial myocardium stimulation by said atrial wall electrode, to a second mode, for effecting atrial myocardium stimulation by said at least one floating atrial electrode, upon perceiving atrial signals that are evaluated as being high-frequency irregularities such as auricular fibrillation or atrial tachycardias as on the basis of inadmissibly high signal frequencies.
2. The pacemaker arrangement as set forth in claim 1 wherein stimulation is effected by the floating atrial electrode at high frequency with a cycle length of between about 30 and 100 ms.
3. The pacemaker arrangement as set forth in claim 1 wherein there are provided two or more floating atrial electrodes and two or more ventricular electrodes of said ventricular electrode line.
6. The pacemaker arrangement as set forth in claim 1 wherein the floating atrial electrode performs as a sensor with the circuit for perceiving atrial signals.

7. The pacemaker arrangement as set forth in claim 1 wherein the atrial wall electrode performs as a sensor with the circuit for perceiving atrial signals.
11. The pacemaker arrangement as set forth in claim 2 wherein there are provided two or more floating atrial electrodes and two or more ventricular electrodes of said ventricular electrode line.
17. The pacemaker arrangement as set forth in claim 2 wherein the floating atrial electrode performs as a sensor with the circuit for perceiving atrial signals.
18. The pacemaker arrangement as set forth in claim 3 wherein the floating atrial electrodes perform as sensors with the circuit for perceiving atrial signals.
21. The pacemaker arrangement as set forth in claim 2 wherein the atrial wall electrode performs as a sensor with the circuit for perceiving atrial signals.
22. The pacemaker arrangement as set forth in claim 3 wherein the atrial wall electrode performs as a sensor with the circuit for perceiving atrial signals.
25. The pacemaker arrangement as set forth in claim 6 wherein the atrial wall electrode performs as a sensor with the circuit for perceiving atrial signals.
27. The cardiac pacemaker of claim 1 wherein the atrial wall electrode of the atrial electrode line and the floating atrial electrode of the ventricular electrode line are of about the same physical size.

IX. Evidence Appendix

Exhibit A – Advisory Action dated July 17, 2009.



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/674,279	09/29/2003	Wolfgang Hartung	117163.00090	3123

21324 7590 07/17/2009
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EXAMINER

ALTER, ALYSSA MARGO

ART UNIT	PAPER NUMBER
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3762

NOTIFICATION DATE	DELIVERY MODE
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07/17/2009

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@hahnlaw.com
akron-docket@hotmail.com

Advisory Action Before the Filing of an Appeal Brief	Application No. 10/674,279	Applicant(s) HARTUNG, WOLFGANG	
	Examiner Alyssa M. Alter	Art Unit 3762	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 05 May 2009 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
- b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
- (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ They raise the issue of new matter (see NOTE below);
- (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
- The status of the claim(s) is (or will be) as follows:
- Claim(s) allowed: _____.
- Claim(s) objected to: _____.
- Claim(s) rejected: _____.
- Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/George R Evanisko/
Primary Examiner, Art Unit 3762

Continuation of 11. does NOT place the application in condition for allowance because: The Applicant argues that claim 3 and 11 are supported by the specification through figure 4, four electrodes placed in the atrium of the heart and two electrodes placed in the ventricle. This contention is not clearly depicted in figure 4. Regardless, dependant claim 3 recites "two or more floating atrial electrodes and two or more ventricular electrodes". Therefore, claim 3 recites, at least 3 floating electrodes, one atrial wall electrode and 3 ventricular electrodes. Which, in accordance with the Applicant's description of figure 4, "the present application shows four electrodes placed in the atrium of the heart and two electrodes placed in the ventricle of the heart" does not support the claim limitation of 2 or more additional electrodes placed in the ventricle.

Additionally, the Applicant argues that present application provides written support for the "wall electrode" and "floating electrode" being approximately the same size. The Applicant refers to the drawing, figure 4, of the present invention to provide support since they "appear to be about the same physical size with respects to each other and with respect to the gross dimensions of the heart shown in Fig.4" (page 6, lines 17-18 of Applicants arguments). Additionally Applicant states "Therefore, Applicants do not regard such a claimed attribute to be outside the scope of the present application, Furthermore, there is nothing in the known art to suggest that such an atrial wall electrode and floating atrial electrodes could not be of about the same physical size"(page 6, lines 19-21 of Applicants arguments).

On the contrary to the Applicant's contention, the examiner can not clearly and affirmatively observe the size dimensions of the electrodes provided in figure 4 (the figure is not in 3D also) to confirm the relative size of the electrodes to the heart or the hearts geometry. Furthermore, there is no indication in the specification to acknowledge that the electrodes are drawn to scale and of similar size. In addition, the mere absence of evidence ("nothing in the known art to suggest that such an atrial wall electrode and floating atrial electrodes could not be of about the same physical size") does not affirmatively provide support for such claim limitation. Therefore, the rejections of claims 3, 11 and 27 remain rejected under 112 first paragraph.

Additionally, claims are rejected under 112 2nd. The Applicant argues that the floating electrode line does possess a floating electrode, but that is not in accordance with the claimed limitations. The claims recite a floating electrode lead, but then employ a wall electrode, while the ventricular electrode line includes a floating atrial electrode. Therefore, if the floating atrial line does in fact possess a floating electrode, the examiner encourages the Applicant to place such a limitation in the claim to definitely recite and distinctly claim the subject matter.

As to the 103 rejections, the Applicant argues that Alt et al. does not provide a ventricular electrode line with an floating atrial electrode. The examiner acknowledges this, and states it would be obvious to modify Alt et al. to derive a leaded system with a floating electrode on the ventricular lead. Furthermore, the examiner indicates that it would be obvious to include multiple electrodes on one lead to combine the stimulation functions. The Applicant argues that such combination would not meet the claimed limitations, however the examiner contends that it would be obvious to modify the lead structures to include a floating electrode placed on the ventricular lead and the atrial wall electrode remaining on the atrial lead. Therefore, the modified Alt et al. thus meets the claimed limitations. Finally, the applicant argues that "atrial stimulation (not atrial defibrillation) is performed" in the claims. This argument is not persuasive since atrial defibrillation IS an atrial stimulation. Similarly, the applicant argues that Alt shows a large surface electrode and not a small surface stimulation electrode. This too is not persuasive since the claim does not state "a small surface stimulation electrode" but only an "electrode" for stimulation--which Alt's coil electrodes ARE electrodes for stimulation.

Exhibit B – Final Office Action dated March 5, 2009.



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/674,279	09/29/2003	Wolfgang Hartung	117163.00090	3123

21324 7590 03/05/2009
HAHN LOESER & PARKS, LLP
One GOJO Plaza
Suite 300
AKRON, OH 44311-1076

EXAMINER

ALTER, ALYSSA MARGO

ART UNIT	PAPER NUMBER
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3762

NOTIFICATION DATE	DELIVERY MODE
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03/05/2009

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@hahnlaw.com
akron-docket@hotmail.com

Office Action Summary	Application No. 10/674,279	Applicant(s) HARTUNG, WOLFGANG	
	Examiner Alyssa M. Alter	Art Unit 3762	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 November 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,6,7,11,17,18,21,22,25 and 27 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3,6,7,11,17,18,21,22,25 and 27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 02 July 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Response to Arguments

Applicant's arguments with respect to claims 1-3, 6-7, 11, 17-18, 21-22, 25 and 27 have been considered but are moot in view of the new ground(s) of rejection necessitated by amendment.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 3, 11 and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. As to claims 3 and 11, the specification does not provide support for "two or more floating atrial electrodes and two or more ventricular electrodes of said ventricular electrode line".

As to claim 27 the specification does not provide support for the "atrial wall electrode" and the "floating atrial electrodes" being "about the same physical size".

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 1-3, 6-7, 11, 17-18, 21-22, 25 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear what the Applicant considers to be the “floating atrial electrode line”. Additionally, it is unclear if the “at least one floating atrial electrode line” also possesses a floating atrial electrode in addition to the wall electrode.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

1. Claims 1-3, 6-7, 11, 17-18, 21-22, 25 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alt et al. (US 6,370,427 B1). Alt et al. discloses a pacing and defibrillation system. As seen in figure 4 the system includes an electrode line or lead 63 in the atrium with a wall electrode 64 and a floating electrode 62. Electrode 64, or the wall electrode, is used for sensing and pacing the cardiac activity of the atrium. Electrode 62, or the floating electrode, is used to provide a defibrillation shock to the heart. The wall electrode operates in a first mode by sensing and pacing the atrium of

the heart, while the floating electrode operates in a second mode to provide defibrillation stimulation. Additionally, figure 4 depicts a ventricular electrode line (VDD-electrode line) as lead 66. The lead also possesses a floating electrode 70.

Alt et al. discloses the device substantially as claimed except for placing a floating atrial electrode on the ventricular electrode line (VDD-electrode line). It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the electrode lines and electrode placement to include a floating atrial electrode on the same line as a ventricular electrode since it has been held that forming in one piece an article which has formerly been formed in two pieces and put together involves only routine skill in the art. *Howard v. Detroit Stove Works*, 150 U.S. 164 (see MPEP 2144.04).

Furthermore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the lead electrodes since it was known in the art that such a modification to place multiple electrodes on one lead would provide the predictable results of reducing the quantity of invasive leads placed into the heart.

As to claims 3 and 11, Alt et al. discloses the claimed invention except for the two or more floating atrial electrodes and the two or more ventricular electrodes located on the ventricle electrode line. It would have been obvious to one having ordinary skill in the art at the time the invention was made to include multiple electrodes on the electrode line, since it has been held that mere duplication of the essential working parts of a device involves only routine skill in the art. *St. Regis Paper Co. v. Bemis Co.*, 193 USPQ 8 (see MPEP 2144.04).

Furthermore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the lead electrodes since it was known in the art that such a modification to place multiple electrodes on one lead would provide the predictable results of reducing the quantity of invasive leads placed into the heart.

As to claims 2, 11, 21 and 25, Alt et al. discloses the claimed invention except for the high frequency stimulation with a cycle length of between 30-100 ms. It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the cycle length of the stimulation by Alt et al., since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233 (see MPEP 2144.05).

Furthermore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the cycle length since it was known in the art that such a modification to the cycle length would provide the predictable results of modifying the stimulation to meet specific patient therapy needs and requirements.

As to claims 6, 17-18, Alt et al. discloses the device the claimed invention except for the floating electrode performing as a sensor. It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the defibrillation electrode with a sensing capabilities since it is well known in the art to use dual sensing and stimulating electrodes.

Furthermore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the electrodes since it was known in the art

that such a modification would provide the predictable results of additional sensing to ensure proper detection of cardiac fibrillation.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alyssa M. Alter whose telephone number is (571)272-4939. The examiner can normally be reached on M-F 8am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Angela Sykes can be reached on (571) 272-4955. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/George R Evanisko/
Primary Examiner, Art Unit 3762

/Alyssa M Alter/
Examiner
Art Unit 3762

Exhibit C – U.S. Patent No. 6,370,427 B1 to Alt et al., first considered by the Examiner in the Office Action of April 18, 2008.



US006370427B1

(12) **United States Patent**
Alt et al.

(10) **Patent No.:** **US 6,370,427 B1**
(45) **Date of Patent:** **Apr. 9, 2002**

(54) **METHOD AND APPARATUS FOR DUAL
CHAMBER BI-VENTRICULAR PACING AND
DEFIBRILLATION**

(75) Inventors: **Eckhard Alt**, Ottobrunn (DE);
Lawrence J. Stotts, Lake Jackson;
Richard Sanders, Houston, both of TX
(US)

(73) Assignee: **Intermedics, Inc.**, St. Paul, MN (US)

(*) Notice: Subject to any disclaimer, the term of this
patent is extended or adjusted under 35
U.S.C. 154(b) by 0 days.

(21) Appl. No.: **09/121,523**

(22) Filed: **Jul. 23, 1998**

(51) **Int. Cl.**⁷ **A61N 1/39**

(52) **U.S. Cl.** **607/4; 607/5; 607/9; 607/121;**
607/120

(58) **Field of Search** **607/4, 5, 9, 122,**
607/120, 121

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,033,357 A *	7/1977	Helland et al.	607/122
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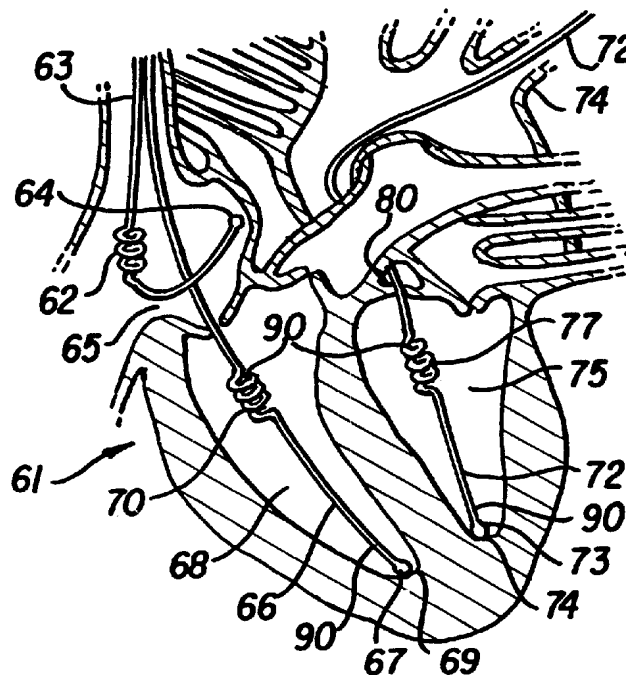
Primary Examiner—George R. Evanisko

(74) *Attorney, Agent, or Firm*—Blank, Rome, Comisky &
McCauley, LLP

(57) **ABSTRACT**

Device and method are disclosed in which leads with pacing and defibrillating electrodes are implanted into both the right and left ventricles of a patient's heart to enable simultaneous pacing of both ventricles to reduce the width of the QRS complex of the patient's cardiac activity to a more normal duration, and, when appropriate, to apply electrical shock waveforms to both ventricles simultaneously for lower energy defibrillation of the ventricles. In applying the defibrillation therapy, the defibrillating electrode in the left ventricle may be used as the anode and the defibrillating electrode in the right ventricle may be used as the cathode, or both ventricular defibrillating electrodes may be the anode and the metal case in which the shock waveform generator is implanted may be the cathode. Implanting a lead with pacing and defibrillating electrodes in the right atrium enables selective pacing and defibrillation of the atria, in which atrial fibrillation is treated by applying the shock waveform across the right atrial and left ventricular defibrillation electrodes.

33 Claims, 2 Drawing Sheets



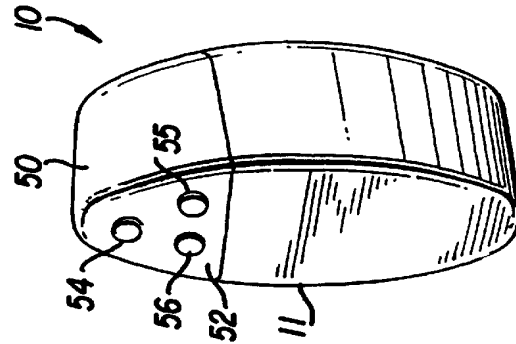
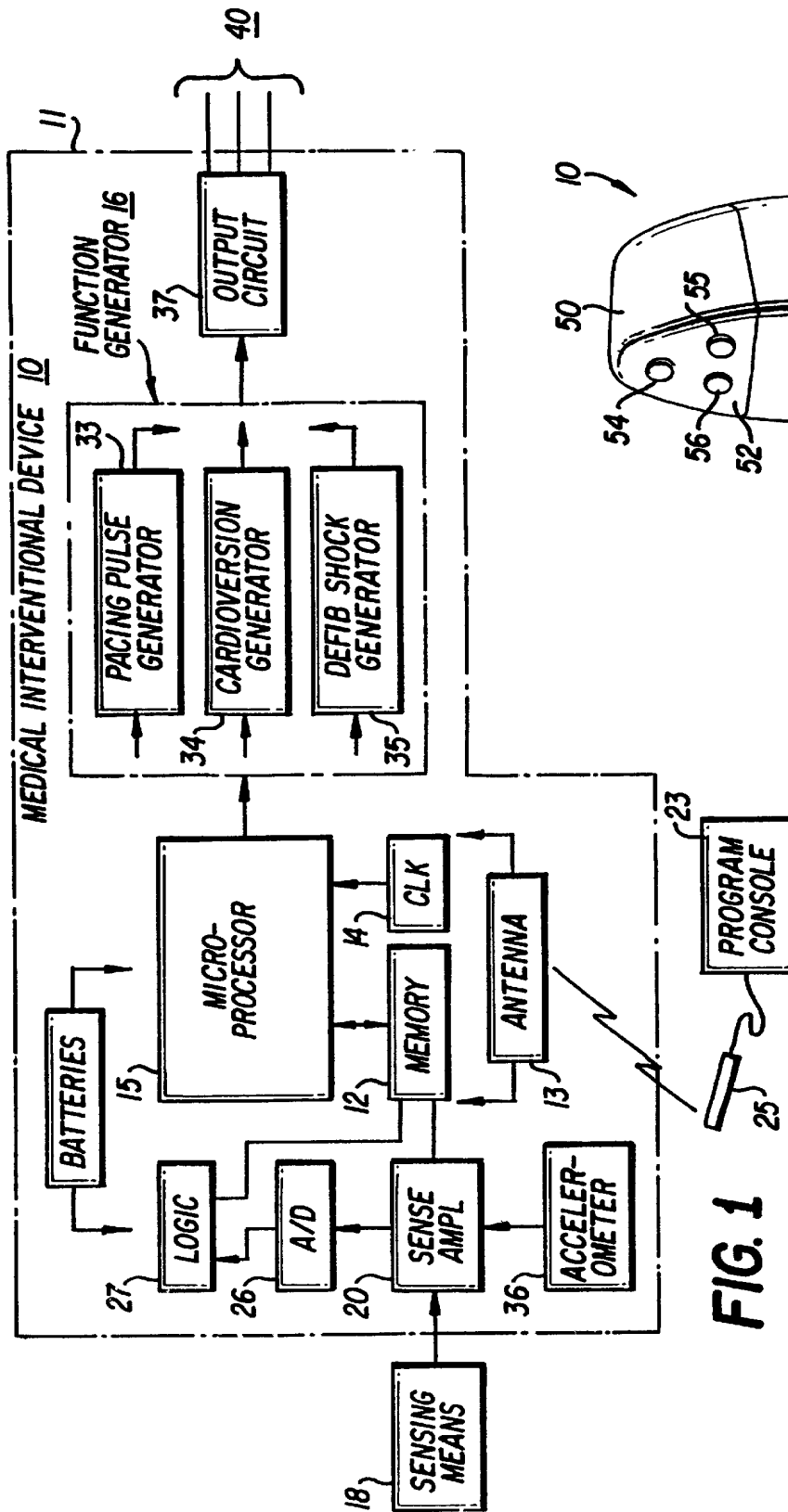


FIG. 2

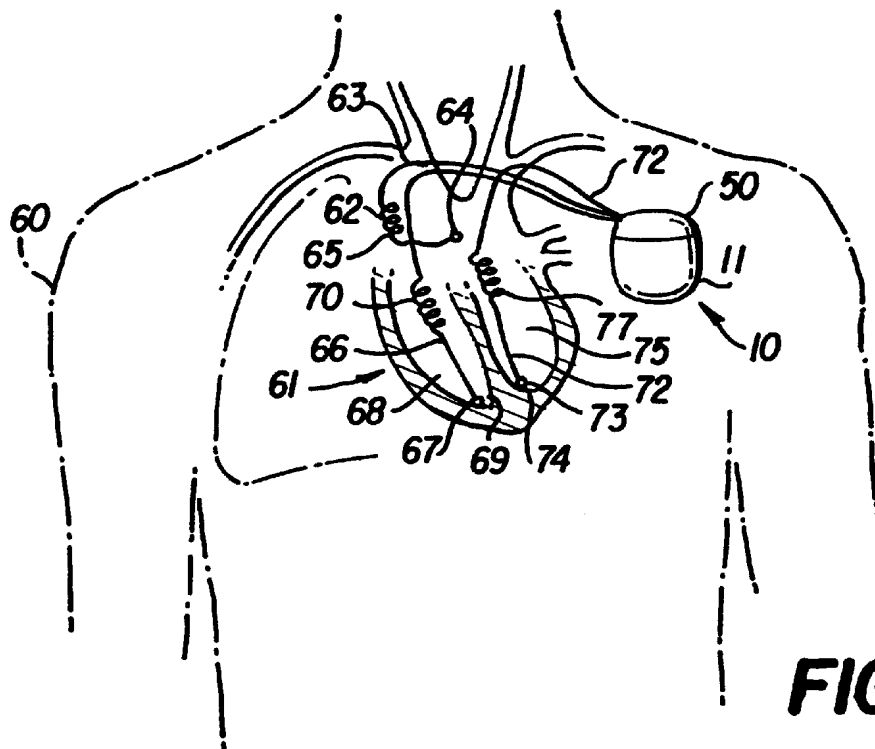


FIG. 3

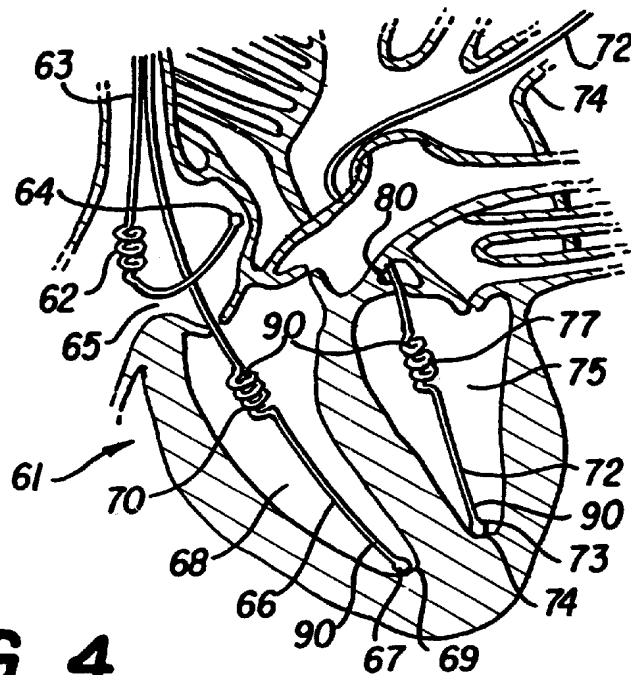


FIG. 4

METHOD AND APPARATUS FOR DUAL CHAMBER BI-VENTRICULAR PACING AND DEFIBRILLATION

BACKGROUND OF THE INVENTION

The present invention relates generally to implantable medical devices for treating cardiac dysrhythmias, and more particularly to a multi-mode device which is adapted to provide bi-ventricular therapy to the patient's heart in response to sensing applicable dysrhythmias.

Progress in medicine is based largely on progress in the technology of devices and apparatus for administering therapy. For example, significant advances in design techniques that have resulted in continuing reductions in the size of implantable defibrillators, including size of the function generator itself as well as in the heart leads associated therewith, have led to a capability to implant defibrillators at considerably lower risk to patients. During the first few years following the advent of implantable defibrillators, implant procedures required general anesthesia and thoracotomy, and the patient was faced with all of the risks associated with opening the chest cavity. The mortality rate of the procedure tended to limit widespread use of the device.

In recent years, with lower defibrillation thresholds (DFTs) and reduction in high voltage capacitor and battery sizes, smaller and more easily implantable devices have been developed, which have allowed this operation to be performed today under only local anesthesia. Smaller diameter and more easily inserted transvenous lead systems have overcome the need for a thoracotomy, and mortality associated with the procedure has been concomitantly reduced to less than one percent. The cosmetic aspects of such an implantation have also improved, with device size and weight allowing it to be implanted in the pectoral region that had previously been reserved for devices capable of only pacing functions, rather than the lower abdomen.

Nevertheless, at least two issues remain to be resolved with respect to present-day implantable defibrillators. For one thing, despite size reduction owing to the aforementioned advances in technology, the devices are still relatively large. At present, the limitations on size reduction are primarily attributable to the magnitude of energy required to achieve successful defibrillation with an adequate safety margin. A capacity for energy delivery of 25 to 32 joules (J), on average, currently remains the standard for implantable defibrillators. This minimum energy requirement mandates production and use of devices ranging from 40 to 50 cubic centimeters (cc) in volume and 80 to 100 grams (g) in weight.

Another issue that remains to be resolved is the provision of a continuously uniform, homogeneous electric field distribution during application of the relatively high energy defibrillating shocks to the heart. Studies performed on animals and humans indicate that to achieve a successful defibrillation with a lowered energy content shock requires a substantially uniform electric field distribution throughout the portion of the mass of cardiac tissue involved in the fibrillation. Lower energy requirement and fewer shocks to achieve a successful defibrillation are important not only from the standpoints of further size reduction and maintenance of an adequate reserve to increase the interval between defibrillator replacements, but also to avoid potential damage to the heart and skeletal frame of the patient that can occur with frequent or repeated application of high energy shocks.

Under typical defibrillator implant conditions, a coil is introduced into the right ventricle to serve as one electrode or pole, and the defibrillator case (or "can," as it is often called in the art) that houses the batteries, capacitors, electronic components and circuitry is used as the second pole for the current path during the defibrillation shock. As noted above, the defibrillator case can now be implanted in the pectoral region, usually on the left side, to provide a more effective defibrillation pathway. This is desirable from the standpoint of the implant technique and the cosmetic aspect, but produces an energy and electric field distribution that is not equal, uniform or homogeneous throughout the region of the heart involved in the fibrillation. Measurements performed by the applicants have demonstrated that during application of a shock waveform using standard case, lead and defibrillation coil placements, a field of significantly lower energy (in volts (v) per centimeter (cm), i.e., v/cm) is present at the apex of the left ventricle compared to certain other regions of the heart such as the right ventricular outflow tract. The average electric field strength in the latter region is five to eight times greater than at the apex of the left ventricle.

In practice, then, because a relatively lower energy field is present at some regions that may be critical to defibrillation, the energy gradient sufficient to achieve successful defibrillation by application of the shock waveform mandates an adequate energy level in those regions and, by extension, a considerably higher electric field density in the normally higher energy field locations as well. The result is a further skewing of the inequality or inhomogeneity of the electric field distribution in the strategically important regions.

In one of its aspects, the present invention provides improvements in lead and electrode placements to assist in developing an equal, homogeneous field distribution during application of a defibrillation shock to the heart.

Another problem encountered with present day defibrillators, however, is that despite their capability to provide adequate therapy for sudden electrical instabilities of the cardiac function, they are not similarly capable of providing therapy for an underlying hemodynamically-compromised ventricular function. This means that the patient may suffer an ongoing deficiency in cardiac output, for example, even though the device is effective in correcting isolated events of fibrillation or pacing dysrhythmias.

Clinical investigation performed on patients who suffer from heart failure (i.e., inability of the heart to pump the required amount of blood) indicates that for a certain subset of these patients simultaneous stimulation of the left and right ventricles may be advantageous. In the cardiac cycle, a P wave of the subject's electrocardiogram (ECG) is produced by a depolarization of the atrial fibers just before they contract, and, when the cardiac impulse reaches the ventricular fibers to stimulate them into depolarization, a QRS complex is produced just before contraction of the ventricular walls. This is followed by a T wave which is indicative of the electrical activity occurring upon repolarization of the ventricular fibers. Simultaneous stimulation of the left and right ventricle would be beneficial therapy to patients whose ECG displays a marked desynchronization in contraction of the two ventricular chambers. In such cases, it is observed that after a right ventricular stimulation, considerable time may elapse for the cardiac impulse to travel from the apex of the right ventricle through the septum and to the free wall of the left ventricle, with the septum contracting earlier than the latter.

Consequently, the mechanical forces of the ventricular contraction are less favorable for an effective hemodynamic

output in such patients. The duration or width of the QRS complex may increase because of an injury to the Purkinje fibers that inhabit and stimulate the ventricular septum and the lateral ventricular walls, and which could therefore increase the time for the impulse to spread throughout the ventricular walls. Patients who display a lack of ventricular synchronization primarily exhibit a wide QRS complex indicative of a bundle branch block—generally a left bundle branch block. Rather than the normal QRS complex width that ranges between 80 to 120 milliseconds (ms), the width of the QRS complex for these patients ranges between 140 and 200 ms.

It is a principal aim of the present invention to provide a method and apparatus for improved hemodynamic performance in patients with heart failure, utilizing an implantable defibrillator of reduced size and increased efficacy which produces a substantially uniform, homogeneous electric field upon application of a defibrillation shock to the heart.

SUMMARY OF THE INVENTION

The present invention provides simultaneous pacing of the left and right ventricles of the patient's heart, and, unlike the prior art in which a pacing lead is inserted into the right ventricle only (through the right atrium and tricuspid valve), a separate pacing lead is also inserted into the left ventricle. Defibrillation coils provided on separate lead wires may be sheathed in respective ones of the two pacing leads for insertion therewith. A defibrillation coil is introduced on a lead into the right ventricle and is seated so that a sensing and stimulating electrode at its distal end resides at the apex of that chamber. An atrial defibrillation coil is inserted on another lead into the right atrium to enable stimulation of the atrial chamber, as appropriate, with pacing pulses and for application of defibrillating shocks. These right chamber (ventricular and atrial) leads enable cardiac pacing stimulation in VVI, VVI-R, DDD, DDD-R, AAI, AAI-R, and other modes, and permit application of defibrillation shocks between the respective coil and the active can or case of the device.

According to the invention, a second ventricular lead is placed in the left ventricle by needle puncture of the arteria subclavia (left subclavian artery) or the brachiocephalic artery, and advancement into the left ventricular chamber through the aortic valve. To avoid interference with the mechanical function of the aortic valve during retrograde passage of this lead into the left ventricle, or thereafter while in place, the lead should be of relatively smaller diameter than traditional ventricular leads (e.g., in a range of 6 to 7 French, or less). Also, its outer surface should be composed of electrically insulative material of very low thrombogenicity (e.g., high performance silicone or polyurethane). Local formation of a thrombus that could embolize and travel to the brain through the aortic valve is additionally avoided by use of platelet (thrombocyte) inhibitors (e.g., preferably ticlopidine, but alternatively or additionally aspirin, GPIIb/IIIa blockers or other inhibitors of the fibrinogen receptor), and by plasmatic coagulation inhibitors (e.g., heparin and hirudin). Such inhibitors are preferably administered for a duration of about one to three months following the surgical procedure. This time period should be adequate to allow a build-up of protective connective tissue around the electrode and also to prevent adhesion of the lead body in the vicinity of the aortic valve.

The left ventricular lead is otherwise of similar construction to the right ventricular lead, and enables pacing stimulation of the left ventricle simultaneously with pacing stimu-

lation of the right ventricle, with resulting improvement in hemodynamics, in large measure by virtue of more organized contraction and avoidance of mitral regurgitation. It is also possible, albeit difficult, to place a lead with a pacing electrode in the left atrium. This is achievable, preferably, by inserting the lead into the left atrium by access from the adjacent distal coronary sinus, or, alternatively, by access through the atrial septum wall from the right atrium. This enables simultaneous pacing of the right and left atria, and synchronization of the simultaneous pacing of the right and left ventricles according to the preset A-V delay, in a DDD mode, plus the capability for bi-ventricular defibrillation.

Most importantly, placement of a defibrillation coil on a lead in the left ventricle allows a considerable reduction of the energy requirement necessary to achieve a successful shock (i.e., termination of ventricular fibrillation, and return to sinus rhythm), with a threshold (DFT) that may be as low as only 2 to 3 joules (J.). To that end, the defibrillation shocks may be applied solely between the two (i.e., right and left) ventricular coil electrodes, and by creating a substantially equal and homogeneous electric field distribution around them through the two ventricular chambers. Alternatively, if individual parameters of thorax geometry and the heart make it necessary or desirable, the shock waveform may be applied between both ventricular coils, operating as one pole, and the device case acting as the other pole. In this alternative configuration, defibrillation is achieved with a somewhat higher DFT than the other, but still considerably below the thresholds seen in the prior art.

Thus, the present invention permits defibrillators with maximum available energy output capability of only 15 joules or less to be implanted with reasonable assurance of successful defibrillation with quite adequate safety margin, even in relatively enlarged hearts. Such low energy requirement means that devices weighing considerably less than 50 grams (g.) and having volumes of less than even 30 cubic centimeters (cc.) can be implemented for this purpose, so that the function generator portion of the device can be sized on the same order as devices that functioned solely as the DDD pacemaker of recent vintage. Hemodynamic improvement attained by simultaneously pacing the left and right ventricles also reduces the occurrence of fibrillation, and thus, the need for defibrillation.

In one aspect of the invention, an implantable medical interventional device is adapted to provide therapy to a patient in whom the device is implanted to treat cardiac dysrhythmias. The device includes function generating means for providing a plurality of functions corresponding to different levels of therapy for treatment of sensed dysrhythmias, including a pulse generator adapted for pacing the patient's heart by generating stimulating electrical pulses therefor. A pair of thin leads is coupled to the pulse generator and sized for insertion respectively into the left and right ventricles of the patient's heart when the device is implanted, for application of the stimulating electrical pulses thereto. Each of the leads includes an electrode located on the respective lead for positioning in stimulating relation to cardiac tissue in a respective one of the ventricles and, when energized together by the pulse generator, to simultaneously pace the left and right ventricles.

The lead adapted for insertion into the left ventricle includes an insulative sheath composed of a material of low thrombogenicity, such as a material selected from a group which includes high performance silicone and polyurethane. Also, the insulative sheath is coated at least in part with a biodegradable material to inhibit thrombus formation on the respective lead. The biodegradable material coating may be

impregnated with at least one platelet inhibitor (preferably, iloprost) for timed release during disintegration of the coating. The coating may additionally or alternatively be impregnated with a plasmatic coagulation inhibitor such as heparin or hirudin for timed release.

The function generator includes a shock generator adapted for defibrillating the patient's heart by generating higher voltage electrical shock waveforms. Each of the leads includes a defibrillation coil coupled to the shock generator and located on its lead to be positioned within a respective ventricle to apply an electrical shock waveform to establish a substantially homogeneous electric field of sufficient electrical energy through the ventricles for defibrillation thereof. The defibrillation coils constitute defibrillation poles, and when energized simultaneously the defibrillation coil in the left ventricle is the anode and the defibrillation coil in the right ventricle is the cathode. Alternatively, the ventricular defibrillation coils constitute a single defibrillation pole and are energized simultaneously as an anode, and the metal case within which the function generator is housed constitutes a second defibrillation pole which is energized together with the defibrillation coils as a cathode. An atrial pacing lead includes a pacing electrode coupled to the pulse generator, and a defibrillation coil adapted to be positioned within the right atrium and coupled to the shock generator for defibrillation of the atria.

A variation of the invention is implemented in an implantable pacemaker that includes a pulse generator, a right ventricular pacing lead with an electrode coupled to the pulse generator for positioning in the right ventricle to deliver stimulating pacing pulses from the generator thereto, a left ventricular pacing lead with an electrode coupled to the pulse generator for positioning in the left ventricle to deliver stimulating pacing pulses from the generator thereto, and means for applying selected ones of the stimulating pacing pulses to the right and left ventricular pacing leads for stimulating the ventricles simultaneously. The pacemaker also includes an atrial pacing lead with an electrode coupled to the pulse generator and positioned in the right atrium to deliver stimulating pacing pulses thereto, and means for applying selected ones of the stimulating pacing pulses to the atrial pacing lead, timed for stimulating the atria.

A variation of the invention is implemented in an implantable defibrillator, which includes a shock generator for generating electrical shock waveforms, a right ventricular lead with a defibrillation electrode coupled to the shock generator for positioning in the right ventricle to deliver electrical shock waveforms thereto, a left ventricular lead with a defibrillation electrode coupled to the shock generator for positioning in the left ventricle to deliver electrical shock waveforms thereto, and means for selectively applying electrical shock waveforms of predetermined energy content simultaneously to the right and left ventricular defibrillation electrodes to establish a substantially homogeneous electric field distribution in the ventricles for defibrillation thereof. A right atrial lead of the defibrillator includes a defibrillation electrode coupled to the shock generator for positioning in the right atrium to deliver electrical shock waveforms thereto, and the selectively applying means applies the electrical shock waveforms between the right atrial defibrillation electrode and one of the right ventricular defibrillation electrode, the left ventricular defibrillation electrode, and the metal case of the shock generator, for defibrillation of the atria.

Also according to the invention, a device-implemented method of treating cardiac dysrhythmias is performed with an implantable medical interventional device adapted to

deliver therapy to an implant patient. The device possesses the capability to provide pacing therapy to the patient's heart, and the method includes the steps of sensing a need for ventricular pacing, and responding to the sensed need by delivering pacing pulses simultaneously to both ventricles of the patient's heart. The device-implemented method also includes the steps of sensing ventricular fibrillation, and responding to the sensed ventricular fibrillation by delivering an electrical shock waveform simultaneously to both ventricles to establish an electric field of relatively uniform distribution and sufficient electrical energy through the ventricles for defibrillation thereof.

Another aspect of the invention resides in a method for providing therapy to a patient from a medical interventional device to treat cardiac dysrhythmias, wherein the device performs a plurality of functions corresponding to different levels of therapy for treatment of sensed dysrhythmias. The device responds to each different type of sensed dysrhythmia to generate an electrical waveform therapy among a variety of therapies appropriate to terminate the respective sensed dysrhythmia, including at least electrical pulse and shock waveform therapies therefor. The method includes implanting an electrical lead with an electrode to deliver at least one of the pulse and shock waveform therapies in each of the right and left ventricles, and electrically connecting each lead to the device to enable its electrode to receive at least one of the therapies.

In the method, prior to implanting the lead, at least a portion of the lead to be implanted in the left ventricle is coated with a biodegradable carrier impregnated with a thrombus inhibitor adapted to be time-released into blood in the locality of the portion of the lead in the left ventricle during disintegration of the carrier, to avoid embolization of a thrombus thereat. The method includes selecting the biodegradable carrier to degrade harmlessly in the blood with negligible systemic impact, and selecting at least one of ticlopidine and aspirin as concomitant oral therapy and intravenous or subcutaneous administration of heparin and hirudin, as the thrombus inhibitor. Also, at least one physical parameter of the biodegradable carrier is selected to fix complete disintegration of the carrier within a period of from about one month to about three months from the time of implanting the lead, for time-release of the thrombus inhibitor over the period. The electrical lead is placed in the left ventricle by puncturing one of the subclavian and brachiocephalic arteries, inserting the lead through the puncture, and advancing the lead through the aortic valve into the left ventricle until the electrode is properly located therein. Each ventricular lead includes both a pacing electrode at the distal end of the lead and a defibrillating electrode proximal of the pacing electrode, and advancement of each lead into the respective ventricle includes placing the pacing electrode in proximity to excitable cardiac tissue of the ventricle.

In the method, the right and left ventricles are paced simultaneously, whereby to reduce the duration of the QRS complex of the patient's electrocardiogram. Shocks are applied to the defibrillating electrodes of both the right and left ventricular leads simultaneously, whereby to improve uniformity of the electric field distribution through the ventricles to terminate ventricular fibrillation. And shocks are applied to the defibrillating electrodes of both the right atrial lead and the left ventricular lead simultaneously to terminate atrial fibrillation. Also, the local ECG is detected at the left and right ventricles, and the size, morphology and other characteristics thereof are compared to discriminate the origin of the tachycardia, such as to distinguish ventricular and supraventricular tachycardias from one another.

BRIEF DESCRIPTION OF THE DRAWINGS

The above and still further aims, objects, aspects, features and attendant advantages of the present invention will become apparent from a consideration of the following detailed description of the presently contemplated best mode of practicing the invention, by reference to a preferred embodiment and method, taken in conjunction with the accompanying drawings, in which:

FIG. 1 is a block diagram of an embodiment of an implantable medical interventional device in which the present invention is used;

FIG. 2 is a perspective view of an exemplary header of the implantable medical interventional device of FIG. 1;

FIG. 3 is a partial front view of a patient, shown in phantom, illustrating some of the internal organs including the heart and related vascular system to show the relative locations of the implanted device and its related electrical leads as inserted into the heart; and

FIG. 4 is a simplified anterior view of the human heart showing the placement of the various leads and associated electrodes in the associated vessels and chambers thereof.

DETAILED DESCRIPTION OF THE
PREFERRED EMBODIMENT AND METHOD
OF THE INVENTION

FIG. 1 is a block diagram of an exemplary embodiment of an implantable medical interventional device **10** having capabilities of pacing, cardioversion and defibrillation, all of the components of which may be entirely conventional except as otherwise described herein, in which the present invention may be used. Device **10** includes a function generator **16** for providing a plurality of functions corresponding to different levels of therapy for treatment of dysrhythmias. These may include generating relatively low energy pulse waveforms for pacing therapy including anti-bradycardia and anti-tachycardia pacing, moderate energy shock waveforms for cardioversion therapy, and relatively higher energy shock waveforms for defibrillation therapy. An output circuit of function generator **16** supplies the designated therapy to a set of leads and electrodes for delivering it to designated chambers of the heart. The output circuit may include capacitors and high voltage switches for producing high energy defibrillating shocks, and the electrodes may include the biocompatible metal housing (i.e., the case, or "can") **11** of device **10** as an active electrode, if desired for a particular type of therapy.

Function generator **16** performs its therapy-generating and delivery functions under the control of a microprocessor **15** containing arithmetic, logic, and control circuitry in conjunction with peripheral circuits or subsystems such as memory **12**, clock **14**, etc., as a central processing unit (CPU) for the device. The microprocessor responds to instructions to perform high speed, real-time functions for controlling the operation of the function generator. The memory units may be written to and read from, by telemetry between device **10** and a program console **23** through a wand **25** via antenna **13**, and with related software, so that the microprocessor performs desired functions. These functions may then be varied by means of the programming console, or programmer **23**, by the device manufacturer or the patient's attending physician.

Sensing means **18** within or outside the device housing **11** detects any of various physiologic parameters indicative of the patient's cardiac functions and physical status, to sense dysrhythmias and initiate appropriate response mechanisms

from the device. Sensed parameters may include the patient's electrogram (ECG), heart rate and/or rhythm, status of rest, exercise or activity of the patient (e.g., using an accelerometer **36** within the case **11**, as here, or in its own separate housing), etc., the latter enabling the device **10** to provide a rate adaptive response, as well as other dysrhythmia correction therapies. The sensing means also includes conventional sensors of physiological signals for detecting congestive heart failure, for example.

Sense amplifier circuitry **20** responds to analog input signals **22** from the sensors (sensing means) **18** for processing thereof. The processed signals are converted to digital format by an analog-to-digital (ASD) converter **26** and the digital output is applied to logic circuitry **27** which interacts with microprocessor **15** and memory **12** to execute programmed operating instructions. If the sensed signals are indicative of a dysrhythmia, the device generates the appropriate conventional pacing, cardioverting, or defibrillating electrical waveforms from blocks **33**, **34** or **35**, respectively, of function generator **16** under the control of the microprocessor in response to the specific type of dysrhythmia. When no immediate demand for therapy is being imposed, the microprocessor reverts to a "sleep" mode, to be awakened at any time a therapy requirement is indicated by the sense signals.

Pacing therapy modes may include combinations of single and dual chamber sensing, pacing, and electrical response functions for treating bradycardia and pathologic tachycardia, as well for providing rate-adaptive pacing using the accelerometer **36** as an activity/exercise sensor. Additionally, the device is preferably programmed with memory modes and diagnostics including acquisition of real-time ECG morphology from intracardiac and surface leads, and trends thereof over time, as well as activation of memory or Holter functions in conjunction with various events. For example, the device may be programmed to undergo mode switching from DDD to VVI-R pacing when the patient is experiencing episodes of atrial fibrillation. In that event, the device will switch from DDD to VVI pacing mode automatically when a pathologic atrial tachycardia is detected, and reverts from VVI to DDD operation automatically when physiologic atrial tachycardia is sensed, distinct from the pacing therapy modes selected by programming the device. The atrial ECG morphology, for example, is stored in the form of atrial signals detected prior to, during and after a cardiac dysrhythmia event, and this morphology is retrieved from the implanted device memory at a later time using telemetry and the external program console. This enables interpretation of cardiac activity that led up to the event of interest, the onset of the event, and the response of the patient's heart to the electrical waveform therapy subsequently delivered by the implanted device.

Some therapeutic output waveforms produced by the microprocessor-based function generator **16** may be used to treat more than one rhythm disorder. For example, a burst of pulses may be used for therapy to terminate a tachycardia, or may be one among a hierarchy of therapy responses selectively delivered to perform cardioversion. The waveform representing the appropriate therapy to treat the sensed dysrhythmia within the designed capabilities of device **10**, i.e., pulses, pulse bursts or trains, low energy or high energy shocks, is applied through output circuitry **37** to the applicable heart lead(s) **40** for delivery to preselected locations within the heart. These and other leads may also convey sensed signals from electrodes in or on the heart or at other appropriate locations of the patient's body, and may acquire the ECG morphologies, for return to the device (e.g., for

application to the sense amplifier, or for storage in memory and subsequent retrieval by the programming console via telemetry).

FIG. 2 shows the header 50 of case 11 which incorporates an electrical connector block 52 including receptacles (e.g., 54, 55, 56) for receiving the heart leads 40. The distal ends of the leads are inserted by the physician into the appropriate preselected locations within the patient's heart, and are then connected to the circuitry within the function generator of the device 10 by means of the plug connectors at the proximal ends of the leads, which are inserted into the proper receptacles. It should be emphasized that the connector portion of the header shown in FIG. 2 is not intended to represent a complete connector. As pointed out above, other leads may be plugged into appropriate receptacles for delivering sense signals from the heart or elsewhere in the body, including signals indicative of ECG morphology.

The receptacles 54, 55, 56 of the connector block 52 are sized or otherwise coded to avoid or prevent acceptance of the plug-in connector of any lead other than the proper lead for electrical connection to the internal circuitry of device 10. Once the leads are in place and connected to the device various tests are performed to assure that they are properly seated, such as to detect capture and suitable threshold. Various unique aspects of the connector portion of the device will be discussed in greater detail presently.

FIGS. 3 and 4 represent a phantom partial front view of a patient 60 illustrating the position of the device case 11 implanted in the left pectoral region of the chest, and a more detailed anterior section view of the heart 61 showing the placement of the various heart leads and electrodes. Connected to the function generator 16 of device 10 via connector block 52 is an atrial lead 63 which has its bipolar electrode 64 positioned in close proximity to excitable tissue in the right atrium 65 of the patient's heart 61, for sensing and pacing cardiac activity of the atrium. Right atrial lead 63 has a coil electrode 62 coupled by a separate wire in the sheath of the lead to defibrillator shock generator 35 when the lead is inserted into the proper receptacle of connector block 52.

A ventricular lead 66, with a distal electrode 67 positioned at the apex 69 of the right ventricle 68 when the lead is properly seated, is connected at its proximal end to the proper receptacle of connector block 52 of header 50 of case 11 and is used to sense and pace cardiac activity of the right ventricle. Ventricular lead 66 includes a coil electrode 70, which is on a separate electrical wire, but encompassed in the same sheath as the wire connected to electrode 67, for positioning within the right ventricle when lead 66 is properly seated. Defibrillation shocks are applied to coil electrode 70 in the right ventricle 68 to establish an electric field relative to a counter-electrode outside the heart, which is typically the metal can or case 11 that houses the electronics and batteries of device 10. The location of the case implanted in the left pectoral region of the patient's chest assures that the field will be present over a large part of the mass of the ventricular walls.

According to the present invention, separate pacing leads 72 and 66 are implanted in the left and right ventricles 75, 68, respectively, of the patient's heart to allow the ventricles to be paced simultaneously. For purposes of ventricular defibrillation, each of these ventricular leads also has its own separate defibrillation coil (77, 70, respectively). The right ventricular lead 66 is introduced into the right ventricle in the usual manner by venous access, such as via the vena subclavia either by puncture or by a cutdown of the vena

cephalica. As noted above, this lead is placed with its distal electrode 67 resident at the apex 69 of the chamber, for electrical stimulation to pace the ventricle 68 and, in the event of ventricular fibrillation, to deliver a defibrillation shock to the ventricle, by application of appropriate electrical signals to the proximal end of the lead via the connector block in the header of the implanted defibrillator.

The right atrial lead 63 provides pacing stimulation via electrode 64 to the right atrial chamber 65 from device 10, and also enables defibrillating shocks to be delivered to its associated coil electrode 62 in that chamber from the defibrillator section of the device to which the atrial lead is also connected at the header. These leads allow stimulation in VVI, VVI-R (by means of an activity sensor in the defibrillator), DDD, DDD-R, AAI, AAI-R, and other modes. The defibrillating shocks can be applied between the coil of the respective lead and the active can 11.

According to the invention, a left ventricular lead 72 is inserted into the left ventricle 73 by advancement into the arteria subclavia 74 which is either punctured or exposed by surgical preparation for access to the arterial system. Alternatively, the left ventricular lead may be implanted by puncture of the truncus brachiocephalicus and insertion through that puncture. Another technique is to surgically expose either the subclavian artery or the brachiocephalic artery and to apply a circular tightening suture ("tabakbeutelnaht"). This assists in tightening up the site of entry to avoid internal bleeding, which is especially important where subsequent anti-coagulation measures are employed by use of platelet inhibitors as is more fully explained below.

It is essential that the outer surface of this lead 72 be of very low thrombogenicity, such as by use of high performance silicone or polyurethane insulation, and by other techniques which will be described presently. It is also important that the lead body be of very small diameter, e.g., in a range from less than about 7 F, so as not to compromise the mechanical function of the aortic valve 80 during retrograde passage into the left ventricle 75 or during the valve's operation in the cardiac cycle.

Advanced materials and fabrication techniques have enabled reductions in size of heart lead diameters for implantable defibrillators to a range of 5 to 7 French (1.66 mm to 2.33 mm) from previous sizes that ranged from 9 to 11 French (i.e., 3.00 mm to 3.66 mm). More recent developments in coated wire techniques have made it possible to produce lead diameters in an even smaller range, of from 4 to 6 French (1.33 mm to 2.00 mm). These small sizes make it much easier to insert the defibrillator leads through the vascular system to the heart, and to place the leads and associated electrodes or poles in the desired position(s) in the appropriate chamber(s) of the heart.

The left ventricular lead 72 has a pacing (and sensing) electrode 73 located at its distal end, which is seated at the apex 74 of left ventricle 75 when the lead is properly and fully inserted in place. This lead also has a defibrillation coil electrode 77. After insertion through the puncture opening in the left subclavian artery or the brachiocephalic artery, the lead 72 is inserted by retrograde passage through the aortic valve 80 into the left ventricle 75, as shown more clearly in FIG. 4.

The major concern in placement of a left ventricular lead lies in the potential generation of a thrombus on the defibrillator coil. A locally formed thrombus especially in that location might embolize into the brain and cause a cerebral stroke, death or major disability. While previous lead mate-

rials of choice have been relatively thrombogenic, with standard isolating materials having exhibited several layers of thrombocytes and other thrombotic depositions, particularly at the defibrillator coil, newer surface materials such as iridium oxide coated wires and titanium nitrate coated materials, have demonstrated extremely low thrombogenicity. Therefore, successful placement and maintenance of the left ventricular lead can be achieved with considerably less concern by use of a lead with low thrombogenicity insulation as mentioned above, and having a surface coating of titanium nitrate or iridium oxide, for example, on the electrical wire.

In addition, as mentioned above, a pacing lead may be inserted into the left atrium, either by needle puncture and access to the left atrium through the adjacent distal coronary sinus, which is preferred, or through the atrial septum wall from the right atrium. The purpose is to enable simultaneous pacing of the right and left atrial chambers, and, following an appropriate delay representing the atrioventricular (A-V) delay interval, simultaneous pacing of the right and left ventricles by application of the pacing stimuli to the respective leads.

The additional use of systemically applied heparin (in the peri-operative setting) and especially the use of orally administered ticlopidine as thrombocyte inhibitors over a limited period of time (e.g., from one to three months following the operation) can serve to prevent the incidence of local thrombus formation until protective connective tissue builds up around the electrode. Animal and human studies have demonstrated that a very thin protective layer of connective tissue can be formed in as little as three to six weeks. Monocytes, which are present in the blood, deposit on the surface and convert into fibroblast, which builds this connective tissue. It is essential that the process should take place for a sufficient period of buildup of the connective tissue to shield the foreign body and later leave it as a neutral foreign body, to prevent thrombus formation. This may be assisted as well by application to the lead surface of inhibitors of plasmatic coagulation, such as heparin and hirudin, and by inhibitors of platelet aggregation, such as aspirin, membrane or surface receptor GP (glycoprotein) IIb/IIIa blockers (i.e., platelet inhibitors that act on the GP IIb/IIIa receptor), or other inhibitors of the fibrinogen binding receptor.

These inhibitors may be applied by incorporating them into a biodegradable carrier which is used to coat the surfaces of interest, as disclosed in co-pending U.S. patent application Ser. No. 08/798,333 of E. Alt et al, now U.S. Pat. No. 5,788,979 the specification of which is incorporated by reference herein. According to that invention, the carrier itself is a substance or composition that undergoes continuous degradation or disintegration within the body to self-cleanse the coated surface as well as to release thrombus inhibitors incorporated in the coating. The carrier degrades slowly through hydrolytic, enzymatic or other degenerative processes. Blood components including albumin, adhesive proteins, and thrombocytes are unable to adhere to the protected surface because of the continuous cleansing action along the entire surface. Additionally, the added inhibitors undergo slow release with the controlled degradation of the carrier.

The coating carrier is a synthetic or naturally occurring biodegradable polymer such as aliphatic and hydroxy polymers of lactic acid, glycolic acid, mixed polymers and blends, polyhydroxybutyrates and polyhydroxy-valerates and corresponding blends, or polydioxanon, modified starch, gelatine, modified cellulose, caprolactaine polymers, poly-

acrylic acid, polymethacrylic acid or derivatives thereof, which will not alter the structure or function of the material to which it is superficially applied. The biodegradable polymer disintegrates with consequent slow release of the drugs (i.e., the inhibitors) incorporated therein, while in contact with blood or other body fluids.

The carrier layer (which is represented by reference number 90 in FIG. 4 for the sake of illustration, but which may be restricted to portions of the respective leads at and near the electrodes) is applied in an extremely thin and tightly adherent layer less than about 100 microns (μm) thick—even a coating of only 10 μm —to the surface of the lead. It is prepared as a liquid or semi-liquid phase of the selected carrier material, and applied in a very thin, paint-like layer or multiple layers by dipping or spraying, followed by drying of the carrier. Its disintegration over time may be carefully controlled, and the disintegration makes place without harm to the tissue, blood or other fluids of the body. The selected inhibitors are incorporated in the carrier coating for timed release therefrom as the carrier disintegrates, by virtue of the controlled time of disintegration of the carrier. The time of disintegration may be adjusted by varying the thickness of the carrier coating or of its multiple layer along with and/or as well as by factors such as the biodegradable carrier material(s) selected and the specific time release characteristics of the incorporated drugs. Applying the biodegradable coating in multiple, different layers (i.e., with different inhibitors/additives) of the same or different thickness can provide prolonged action of a particular inhibitor and enable different beneficial actions to occur at predetermined different intervals of time. For example, the innermost coating layer (relative to the lead and/or electrode surface) may be intended to provide the most prolonged action, while the outermost layer is intended primarily for near term response to its initial exposure to blood. After the biodegradable material has completely disintegrated, which may be set as a period of several weeks or months, thrombus formation continues to be inhibited because by the time the controlled period has elapsed the lead will have been coated by connective tissue.

Application of the carrier coating with added anti-inflammatory or anti-coagulant substances therein to the electrode(s) of the lead inhibits a build-up of scar tissue on the electrode at the electrode-myocardial (endocardial) tissue interface in the case of the pacing electrode, or the formation of thrombi in the case of the defibrillation electrode, or at the site of passage through the aortic valve, to prevent adhesion of the lead to the leaflets of the valve. The amount and dosage of the drug(s) incorporated into and released from the biodegradable carrier may be prescribed to suppress the thrombus formation process locally without otherwise affecting normal systemic functions.

With both the left ventricular lead 72 and the right ventricular lead 66 in place, pacing stimulation from the implanted device 10 may be applied simultaneously to both pacing electrodes 73 and 67 of the respective ventricular chambers. By synchronizing the mechanical contraction from the apex of the heart, considerable improvement in hemodynamics can be achieved in many patients. This is partly a result of a more organized contraction, and partly an avoidance of mitral regurgitation, which often additionally compromises the left ventricular function. Hemodynamic improvement has been shown to reduce the occurrence of fibrillation, and thus, the need for defibrillation, with concomitant savings of energy consumption and increased longevity of the implanted device.

Use of pacing electrodes in both the right and left ventricles avoids many problems associated with prior art left

ventricle stimulation. And the retrograde ventricular access through the aorta and aortic valve **80** to the left ventricle **75** is achieved by a relatively simple procedure of puncturing the subclavia or the brachiocephalic artery which can be done under local anesthesia, in avoidance of a need for and risks of major surgical measures.

Moreover, placement of a defibrillation coil **77** in the left ventricle as well as a defibrillation coil **70** in the right ventricle allows defibrillation shocks to be delivered solely between these two electrodes, to considerably reduce the energy requirements of a successful shock. Even where individual parameters of thorax geometry and of the heart within the thorax may necessitate use of the two ventricular coils as a single pole and of the defibrillator case as the other pole, a substantial reduction in the energy consumption needed for defibrillation is achieved. By virtue of creating a substantially equal electric field distribution around the two ventricular electrodes and through the ventricular chambers, it is possible to implant a defibrillator having a maximum available energy output of only 15 joules to achieve successful defibrillation with adequate safety margin, even in patients with an enlarged heart. This means that the implanted device of the invention can be produced with a weight considerably less than 50 grams and a volume of less than 30 cc, which compares favorably in weight and size with the DDD pacing-limited device types which were being implanted only a few years ago. Cosmetic advantages and reduction of patient discomfort are added advantages of the size and weight reductions.

Provision of a coil on the right atrial lead **63** enables treatment of atrial fibrillation, with a capability of four-way application of shocks between the defibrillation coil **62** in the right atrium **65** and defibrillation coil **77** in the left ventricle **75**, or defibrillation coil **70** in the right ventricle **68**, or the case **11**,—or of coil **62** against a combination of defibrillation coils **77** and **70** and case **11** together—to create a relatively homogeneous electric field through the atria.

Additionally, the lead **63** in the right atrium facilitates discrimination between supraventricular tachycardia (originating from outside the ventricle, generally either from the SA node or AV node or the atrium) and ventricular tachycardia. It provides a knowledge of the underlying atrial rhythm as well as of the ventricular rhythm by detecting the local ECG simultaneously at the left and right ventricles and the right atrium, for comparison. If a complete dissociation between the ventricular arrhythmia and the atrial rhythm is found, the diagnosis of ventricular tachycardia would be virtually conclusive. In that case, an anti-tachycardia therapy may be delivered by the device and associated lead(s) to the ventricle. However, if the discrimination algorithm determines the atrium to be the primary source of the present tachycardia, the therapeutic intervention would instead be generated and delivered as appropriate to treat a diagnosed primary atrial tachyarrhythmia.

Although a presently contemplated best mode of practicing the invention has been described herein, it will be recognized by those skilled in the art to which the invention pertains from a consideration of the foregoing description of a presently preferred embodiment, that variations and modifications of this exemplary embodiment and method may be made without departing from the true spirit and scope of the invention. Accordingly, it is intended that the invention shall be limited only by the appended claims and the rules and principles of applicable law.

What is claimed is:

1. An implantable medical interventional device adapted to provide therapy to a patient to treat cardiac dysrhythmias,

said device comprising a pulse generator and a shock generator for providing a plurality of functions corresponding to different levels of therapy including pulse, low energy and high energy shock waveforms configured to terminate respective dysrhythmias; said pulse generator adapted for pacing the patient's heart by generating stimulating electrical pulses therefor; and a pair of thin leads dimensioned for insertion respectively into the left and right ventricles of the patient's heart when said device is implanted, said pair of thin leads being coupled to said pulse generator and said pulse generator being adapted to energize said pair of thin leads in unison for simultaneous application of said stimulating electrical pulses to the left and right ventricles when said pair of thin leads are inserted respectively therein, each of said leads including a respective electrode adapted to be positioned in stimulating relation to cardiac tissue in a respective one of said ventricles when said leads are inserted therein and, when said leads are energized in unison by said pulse generator, to simultaneously pace said left and right ventricles; the lead dimensioned for insertion into the left ventricle having an insulative sheath composed of a material of low thrombogenicity and coated at least in part with a biodegradable material to inhibit thrombus formation on the respective lead.

2. The device of claim 1, wherein said material of low thrombogenicity is selected from the group consisting of silicone and polyurethane.

3. The device of claim 1, wherein said biodegradable material coating includes at least one platelet inhibitor incorporated therein for timed release during disintegration of said coating.

4. The device of claim 3, wherein said at least one platelet inhibitor is iloprost.

5. The device of claim 3, wherein said biodegradable material coating further includes a plasmatic coagulation inhibitor incorporated therein for timed release during disintegration of said coating.

6. The device of claim 5, wherein said plasmatic coagulation inhibitor is selected from the group consisting of heparin and hirudin.

7. An implantable medical interventional device adapted to provide therapy to a patient to treat cardiac dysrhythmias, said device comprising a pulse generator and a shock generator for providing a plurality of functions corresponding to different levels of therapy including pulse, low energy and high energy shock waveforms configured to terminate respective dysrhythmias; said pulse generator adapted for pacing the patient's heart by generating stimulating electrical pulses therefor; and a pair of thin leads dimensioned for insertion respectively into the left and right ventricles of the patient's heart when said device is implanted, said pair of thin leads being coupled to said pulse generator and said pulse generator being adapted to energize said pair of thin leads in unison for simultaneous application of said stimulating electrical pulses to the left and right ventricles when said pair of thin leads are inserted respectively therein, each of said leads including a respective electrode adapted to be positioned in stimulating relation to cardiac tissue in a respective one of said ventricles when said leads are inserted therein and, when said leads are energized in unison by said pulse generator, to simultaneously pace said left and right ventricles; said shock generator being adapted for defibrillating the patient's heart by generating higher voltage electrical shock waveforms therefor; and each of said pair of leads further including a defibrillation coil coupled to said shock generator and adapted to be positioned within a respective one of said ventricles and, when energized by said

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shock generator, for applying an electrical shock waveform to establish a substantially homogeneous electric field of sufficient electrical energy in the ventricles for defibrillation thereof.

8. The device of claim 7, wherein the defibrillation coils on respective ones of said pair of leads constitute defibrillation poles adapted to be energized simultaneously with their respective leads so that the defibrillation coil on the lead adapted to be positioned in the left ventricle is the anode and the defibrillation coil on the lead adapted to be positioned in the right ventricle is the cathode.

9. The device of claim 7, including a metal case housing said function generator, and wherein the defibrillation coils on said pair of leads constitute a defibrillation pole adapted to be energized simultaneously with their respective leads to act as an anode, in conjunction with said case constituting a defibrillation pole adapted when energized together with said defibrillation coils to act as a cathode.

10. The device of claim 7, further including an atrial pacing lead coupled to said pulse generator, said atrial pacing lead including a right atrial defibrillation coil, said right atrial defibrillation coil being coupled to said shock generator for defibrillation of the atrial chambers.

11. An implantable defibrillator, comprising a shock generator for generating electrical shock waveforms, a right ventricular lead including a defibrillation electrode coupled to said shock generator and adapted to be positioned in the right ventricle of a patient's heart for delivery of electrical shock waveforms thereto, a left ventricular lead including a defibrillation electrode coupled to said shock generator and adapted to be positioned in the left ventricle of the patient's heart for delivery of electrical shock waveforms thereto, and means for selectively applying said electrical shock waveforms of predetermined energy content simultaneously to said right and left ventricular defibrillation electrodes to establish a substantially homogeneous electric field distribution in the ventricles for defibrillation thereof.

12. The defibrillator of claim 11, including a metal case for said shock generator, and wherein said selectively applying means is adapted to apply said electrical shock waveforms either between said right and left ventricular defibrillation electrodes as separate poles, or between said right and left ventricular defibrillation electrodes as one pole and said metal case as another pole, for defibrillation of the ventricles.

13. The defibrillator of claim 11, further comprising a metal case for said shock generator, a right atrial lead including a defibrillation electrode coupled to said shock generator and adapted to be positioned in the right atrium of the patient's heart for delivery of electrical shock waveforms thereto, and wherein said selectively applying means is adapted to apply said electrical shock waveforms between said right atrial defibrillation electrode and one of said right ventricular defibrillation electrode, said left ventricular defibrillation electrode, and said metal case, for defibrillation of the atria.

14. The defibrillator of claim 11, further comprising a pacing pulse generator of stimulating pacing pulses, separate pacing electrodes on each of said right and left ventricular leads respectively coupled to said pulse generator and adapted to be positioned respectively in the right and left ventricles of the patient's heart for selective delivery of stimulating pacing pulses simultaneously thereto, and an atrial pacing lead including an electrode coupled to said pulse generator and adapted to be positioned in the right atrium of the patient's heart for selective delivery of stimulating pacing pulses thereto.

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15. A device-implemented method of treating cardiac dysrhythmias with an implantable medical interventional device adapted to deliver therapy to an implant patient, wherein the device possesses the capability to provide at least pacing therapy to the patient's heart, said method including the steps of:

- sensing a need for ventricular pacing; and
- responding to said sensed need by delivering pacing pulses simultaneously to both ventricles of the patient's heart; and

wherein said device possesses the capability to provide a plurality of functions corresponding to different therapies for treatment of dysrhythmias, and further including the steps of:

- sensing ventricular fibrillation; and
- responding to said sensed ventricular fibrillation by delivering an electrical shock waveform simultaneously to both ventricles of the patient's heart to establish an electric field of relatively uniform distribution and sufficient electrical energy simultaneously in the ventricles for defibrillation thereof.

16. The device-implemented method of claim 15, including

- delivering sense signals indicative of ventricular fibrillation to said device from separate right and left ventricular leads coupled thereto, and

- delivering electrical shock waveforms simultaneously to said right and left ventricular leads from a shock generator of said device.

17. The device-implemented method of claim 15, further including the steps of:

- sensing atrial fibrillation; and
- responding to said sensed atrial fibrillation by delivering an electrical shock waveform between the right atrium and selectively either of the right and left ventricles of the patient's heart to establish an electric field of sufficient electrical energy through the atrium for defibrillation thereof.

18. The device-implemented method of claim 15, including

- delivering sense signals indicative of ventricular fibrillation to said device from separate right and left ventricular leads coupled thereto,

- delivering sense signals indicative of atrial fibrillation to said device from a right atrial lead coupled thereto, and
- delivering electrical shock waveforms from a shock generator of said device to said right atrial lead and said right and left ventricular leads as necessary for defibrillation.

19. An implantable medical interventional device adapted to provide therapy to a patient to treat cardiac dysrhythmias, said device comprising therapy-providing apparatus responsive to different types of dysrhythmia for providing a level of therapy appropriate respectively thereto, including electrical pulse and shock waveforms of sufficiently high energy content to pace and defibrillate respectively; and therapy-application apparatus for application of therapy simultaneously to both ventricles of the patient's heart, including a right ventricular lead and a left ventricular lead each including a pacing electrode and a defibrillating electrode separately coupled to said therapy-providing apparatus.

20. A method for providing a patient with an implanted medical interventional device to treat cardiac dysrhythmias, wherein the device performs a plurality of functions corresponding to different levels of therapy for treatment of

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different types of dysrhythmias, and responds to each different type of dysrhythmia to generate any of a plurality of electrical waveform therapies, including at least electrical pulse and shock waveform therapies, appropriate to terminate the respective sensed dysrhythmia, the method comprising the steps of implanting said device in the patient, implanting an electrical lead in the patient that includes an electrode for delivering at least one of said pulse and shock waveform therapies from the device in each of the right and left ventricles of the patient's heart, and electrically connecting each lead to said device to enable said electrode thereof to receive at least one of the therapies; and prior to implanting the lead, the step of coating at least a portion of the electrical lead to be implanted in the left ventricle with a biodegradable carrier impregnated with a thrombus inhibitor adapted to be time-released into blood in the locality of said portion of the lead in the left ventricle during disintegration of said carrier, to avoid embolization of a thrombus thereat.

21. The method of claim 20, including the step of selecting the biodegradable carrier to degrade harmlessly in the blood with negligible systemic impact, and selecting the thrombus inhibitor from the group consisting of ticlopidine, aspirin, heparin, and hirudin.

22. The method of claim 21, including the step of selecting at least one physical parameter of the biodegradable carrier to fix complete disintegration thereof within a period of from about one month to about three months from the time of implanting the lead, for time-release of the thrombus inhibitor over said period.

23. A method for providing a patient with an implanted medical interventional device to treat cardiac dysrhythmias, wherein the device performs a plurality of functions corresponding to different levels of therapy for treatment of different types of dysrhythmias, and responds to each different type of dysrhythmia to generate any of a plurality of electrical waveform therapies, including at least electrical pulse and shock waveform therapies, appropriate to terminate the respective sensed dysrhythmia, the method comprising the steps of implanting said device in the patient, implanting an electrical lead that includes an electrode for delivering at least one of said pulse and shock waveform therapies from the device in each of the right and left ventricles of the patient's heart, and electrically connecting each lead to said device to enable said electrode thereof to receive at least one of the therapies; and, wherein the step of implanting the electrical lead in the left ventricle includes puncturing one of the subclavian and brachiocephalic arteries, inserting the lead through the puncture, and advancing the lead through the aortic valve into the left ventricle until said electrode is properly located therein.

24. The method of claim 23, wherein each said ventricular lead includes both a pacing electrode at the distal end of the lead and a defibrillating electrode proximal of the pacing electrode, and the step of advancing the lead through the aortic valve into the left ventricle includes placing the pacing electrode in proximity to excitable cardiac tissue of the left ventricle.

25. The method of claim 24, including the step of applying pulse therapy to the pacing electrodes of both the right

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and left ventricular leads for pacing the ventricles simultaneously, whereby to reduce the duration of the QRS complex of the patient's electrocardiogram.

26. The method of claim 24, including the steps of sensing ventricular fibrillation and thereupon applying shock waveform therapy to the defibrillating electrodes of both the right and left ventricular leads simultaneously, whereby to improve uniformity of the electric field distribution through the ventricles to terminate the ventricular fibrillation.

27. The method of claim 26, wherein the step of applying said shock waveform therapy to the defibrillating electrodes of both the right and left ventricular leads simultaneously includes applying said shock waveform therapy to the defibrillating electrode in the left ventricle as the anode and to the defibrillating electrode in the right ventricle as the cathode.

28. The method of claim 26, wherein said device is implanted in a pectoral region of the patient, and the step of applying said shock waveform therapy to the defibrillating electrodes of both the right and left ventricular leads simultaneously includes applying said shock waveform therapy to said defibrillating electrodes in the ventricles as the anode and to an electrically conductive case in which the therapy generator of said device is housed as the cathode.

29. The method of claim 24, including the steps of implanting an electrical lead with a pacing electrode and a defibrillating electrode thereon in the right atrium of the patient's heart, and applying said shock waveform therapy to the defibrillating electrodes of both the right atrial lead and the left ventricular lead simultaneously to terminate atrial fibrillation.

30. The method of claim 29, including the step of selecting leads to be implanted in the right atrium, right ventricle, and left ventricle of the patient's heart which are covered with an insulating sheath selected from a group comprising silicone and polyurethane, and in which the sheath is coated with a material selected from the group consisting of iridium oxide and titanium nitrate.

31. The method of claim 24, including the steps of detecting the local ECG at the left and right ventricles, and comparing the characteristics of size and morphology thereof for diagnosis of cardiac activity from which to discriminate ventricular and supraventricular tachycardias from one another.

32. The method of claim 23, including the steps of administering a platelet inhibitor into the patient's vascular system for a limited period of time to facilitate healing and a build-up of connective tissue on electrodes of the lead implanted in the left ventricle to avoid interference with operation of the aortic valve.

33. A method for providing therapy to a patient from a medical interventional device adapted to be implanted to treat cardiac dysrhythmias, comprising the steps of simultaneously stimulating the right and left ventricles of the patient's heart to perform ventricular pacing for enhancing hemodynamics, and defibrillating the heart by applying electrical defibrillation shocks to a point in the left ventricle to terminate ventricular fibrillation.

* * * * *

Exhibit D – Excerpts from the Text “Implantable Defibrillator Therapy: A Clinical Guide” by Philip D. Henry and Antonio Pacifico, Texas Arrhythmia Institute, Houston, Texas.

Implantable Defibrillator Therapy:

A Clinical Guide

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Chapter 3

DEFIBRILLATOR LEADS

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INTRODUCTION

The "nonthoracotomy" era of device therapy begun with the pioneering work of Furman and Schwedel (1) (1959) and a group of investigators in Stockholm (1963) (2). In the Swedish series of 40 patients, the transvenous leads consisted of twinned stainless steel conductors surrounded by polyethelene tubing (2). Polyethylene, in addition to being too stiff, was soon found to degenerate in vivo. It was rapidly replaced by silicone rubber, which initiated the modern era of transvenous leads. Although lead designs have undergone major advances over the last four decades, it is fair to state that highly reliable lead insulators remain an elusive objective. In the recent past, use of new insulators, polyether urethanes (Pellethane 80A) in particular, accounted for many lead failures (3-8). In the new millenium, nearly four decades after its introduction, silicone rubbers for lead insulation remain a dominant material. However, innovative lead designs using combinations of insulating materials have recently undergone promising clinical evaluation (4-8). Here, we briefly review major components of modern defibrillator leads. Specific lead models and their characteristics are covered in the previous chapter.

PROBLEMS OF LEAD DESIGN

It is often stated that leads are the weak link or indeed "dark side" of device therapy and that advances in lead design have lagged behind those of pacemaker and ICD generators (8-10). However, it is important to recognize that electrode design presents fundamentally different bioengineering and manufacturing problems compared with solid state

electronics as used for generators. Leads are subjected yearly to millions of mechanical stress/strain cycles generated by cardiac, respiratory, and other body motions. They must contend with problems of blood compatibility including protein adsorption, platelet adhesion, leukocyte activation, thrombosis, and chemical attack from trace-metal catalyzed oxidative reactions. In prosthetic heart and cardiac valve engineering, severe problems created by the degradation of mechanically stressed, blood-exposed elastomers could be circumvented by resorting to rigid components (rotary blood pumps, disk valves), a strategy not applicable to lead design. Unlike prostheses supporting mainly mechanical functions, leads must additionally ensure a critical electric continuum function between excitable cells and electrodes. Electric sensing must allow the foolproof detection of weak myocardial electric signals and yet reject "far field signals" (often not so far) originating in contiguous cardiac chambers, skeletal muscle, and the surrounding environment (see chapter on electromagnetic interference, EMI). Thus, the device assembly represents the union of two contrasting designs, hermetically sealed solid state electronics and its antithesis, mechanically and chemically challenged loose wire technology.

CONNECTORS AND ADAPTERS

The adoption of uniform connector standards for pacemakers (IS-1, International Standard ISO 5841.3:1992) and later for defibrillators (DF-1, International Standard ISO 11318:1993) was an important step to facilitate device therapy. However, there remains a disturbing variability in tolerances between connector dimensions and header checkpoints (10). Lead incompatibilities have occurred, although manufacturers observed IS-1 standards (10,11). Because of the previous heterogeneity in connector and header designs, we recommend consultation with manufacturers before replacing old generators.

Although the lead-to-header interface represents a vulnerable site of the ICD assembly, current lead connector designs appear to have accomplished a satisfactory degree of reliability (12). Nevertheless, lead failure related to insulator or conductor problems near the connector is not rare (13,14).

Adapters should be avoided whenever possible and should never be part of a newly implanted system. Some adapters have been reported to have extraordinarily high failure rates (15-17). For instance, adapters LA-201 (15) and 366-08 (16) had estimated failure risks of 28% and 64% within mean follow-ups of 21 and 32 months.

YOKES

The branching of the body of multipolar ICD leads into two to three terminal lead arms are called yokes. In defibrillator leads with integrated bipolar pacing, the conductor to the distal high voltage coil serving also as a

pace/sense anode is bifurcated within the yoke into two conductors, one leading to the bipolar pace/sense connector arm, the other to the high voltage coil connector arm. There is a remarkable paucity of published data on the performance of yokes acting as bifurcation and trifurcation structures. It is unclear how often lead failures within ICD pockets, a frequent site of lead failure (18,19), involve the yokes.

INSULATORS

Compared with unipolar and even bipolar pacemaker leads, defibrillator leads are more complex because of the addition of one or two high voltage coils. ICD leads with true (dedicated) bipolar pace/sense electrodes and single or dual high voltage coils have three or four conductor lumens. Compared with simple unipolar pacing electrodes, modern ICD leads are assembled from 6 to 10 times as many components, a complexity inviting increased failure rates. Insulator material must not only insulate conductors, but must join the different components to produce lead bodies with acceptable mechanical properties, biocompatibility, and biostability. Three architectural strategies have been generally used to accommodate multiple conductors within lead bodies: 1) parallel or side by side lumens (*"multilumen design"*), 2) concentric tubings separating conductor coils in concentric array (*"coaxial design"*), and 3) coated wires parallel-wound into single coils (*"coradial design"*) (Table 1, Figure 1). These various designs make different demands on lead insulation. The use of coated wire technology and coradial designs is currently limited to pacemaker leads.

Silicone Rubbers

During the 1960ies, silicone rubber (Dow Corning MDX40-4515-50A) gained rapidly in popularity as an insulating material for pacemaker leads. Silicone has excellent biostability and biocompatibility, but suffers from mechanical fragility. Because of its low tear strength, silicone lead bodies use relatively thick insulating layers that tend to produce bulky and stiff leads. During the late 1970ies, a new mechanically stronger silicone formulation (Dow Corning ETR Q747-80A) was introduced and side-by-side twin conductor designs were replaced by coaxial bipolar leads. However, coaxial leads made of silicone still often exceeded F 7 diameters. In recent years, silicone rubber remained the dominant insulator material for nearly all marketed defibrillator leads. In triple and quadruple parallel lumen designs (Endotak leads, Guidant/CPI; Sprint Quattro, Medtronic; Kainox, Biotronik), bodies of dual coil defibrillation leads still exceed an 8 F diameter (>2.7 mm), although a similar lead in development (Vectra 1570 and 1580, St. Jude) will have a 6.7 F isodiametric diameter. At lead body-to-coil electrode junctions, some "nonisodiametric" leads (e.g., Endotak Endurance EZ, CPI-Guidant) have silicone sleeves (3.33 mm or 10 F)

DEFIBRILLATION ELECTRODES

Single Right Ventricular Coil (e.g., Platinum/Iridium)
Dual Right Ventricular and Superior Vena Cava Coils

PACE/SENSE ELECTRODES

Microtip High Impedance Cathode
Cathode with Microporous Low-Polarization Surface (e.g., Titanium Nitride)
Steroid Elution (Dexamethasone Sodium Phosphate)
Independent Ring Anode (True/Dedicated Bipolar System)
Distal Defibrillation Coil Serves as Pace/Sense Anode (Integrated Bipolar System)

LEAD BODY

Silicone Rubbers (Modified Surfaces to Reduce Friction)
Silicone Core with Polyurethane or Polyvinylpyrrolidone (PVP) Coating/Overlays
Channels for Stress Absorption ("Empty" or "Crush Lumens")
"Isodiametric" (or Non-Isodiametric) Design

CONDUCTOR

Conductor to Tip Electrode is a Coil Forming the Stylet Pathway
Coaxial (Concentric) Coils; Inner Coil to Tip Electrode Forms the Stylet Pathway
Multifilar Nickel/Cobalt Alloy (MP35N^a) Cables
"Redundant" Cable Insulation (Overlays of ETFE or PTFE^b)

FIXATION

Passive (Tines)
Active Retractable (or Nonretractable) Metal Helix
Electrically Active (or Inactive) Helix

CONNECTOR PINS

IS-1 In-Line Bipolar Pace/Sense Pin
DF-1 Defibrillation Pin

^a MP35N, a fatigue- and corrosion-resistant alloy, contains nickel (35%), cobalt (35%), chromium (20%), and molybdenum (10%). Drawn Brazed Strands (DBS) and Drawn Brazed Tubes (DBT) made of MP35N form single wires that may incorporate cores of silver to reduce electric impedance. Multifilar cables as used for ICD lead conductors are made of several DBS or DBT wires.

^b ETFE: ethylenetetrafluoroethylene; PTFE: polytetrafluoroethylene (Gore-TexTM)

Medtronic Sprint Quattro® (Quadrupolar Defibrillator Lead)

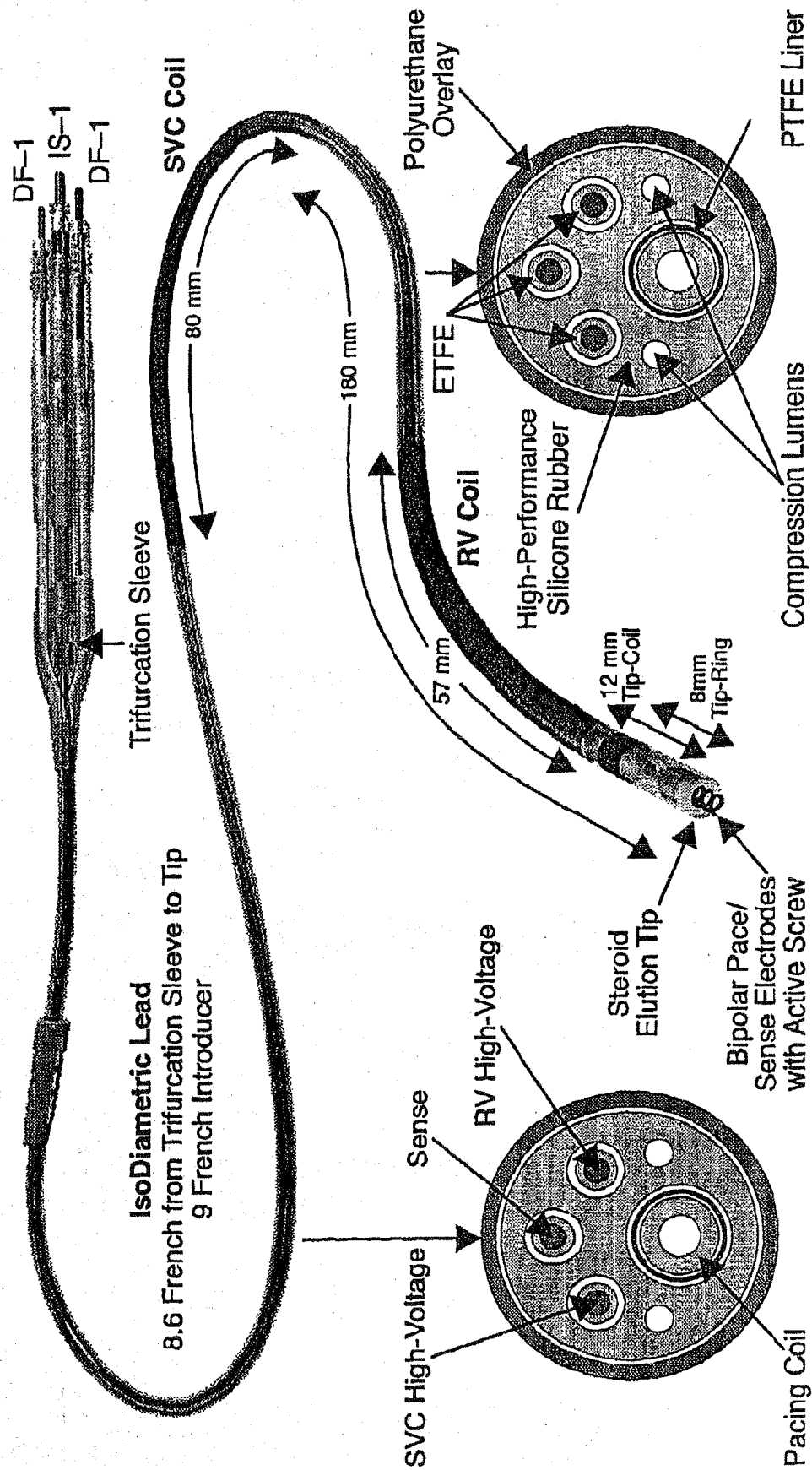


Figure 1. Example of an Advanced Defibrillation Lead

overlapping the junctions, demanding 13 F introducers with guidewire. Dual coil defibrillator leads from other manufacturers have similar maximum lead diameters (Medtronic Sprint 6942, 3.1 mm; St. Jude SPL, 3.6 mm). Most marketed single coil leads are not appreciably thinner than dual coil leads. Silicone surfaces have a relatively high wet friction coefficient which has been partly overcome by various treatments (see below). The adhesive surface of untreated silicone and stiffness of thick silicone lead bodies invite thrombosis, endothelial trauma, and resultant endothelial overgrowth and fibrous mural entrapment of entire lead segments. Incorporation of lead insulators into endovascular surface layers renders lead extraction traumatic and risky (see chapter "ICD lead system dysfunction, diagnosis and therapy"). Forceful extractions of leads adherent to tricuspid valve structures have resulted in severe valve damage (20). Therefore, insulators and defibrillation coils for leads in development need to be tested with special attention to the risk of lead extraction, a procedure of increasing clinical importance (see chapter "ICD lead system dysfunction, diagnosis and therapy" for more detail). It is hoped that the design of thinner, flexible, and lubricious defibrillation leads (about 6 F) will make lead extraction easier in the near future.

Polyurethanes

Polyurethanes, elastomers occurring in numerous formulations, were introduced for use as lead insulators in 1978. Selected polyether polyurethanes were very attractive because of their high tensile strength, high flexibility, relatively slippery surface (low coefficient of friction), good biocompatibility, low thrombogenicity, and noncarcinogenicity. Because of their favorable mechanical properties, polyurethanes allowed the construction of thinner leads compared with silicone leads. Leading manufacturers made extensive use of polyurethanes in the early 1980ies. Unfortunately, about 4-5 years after their clinical introduction, polyether polyurethane (formulation Pellethane 2363-80A) was noted to undergo significant in vivo degradation. The elastomer deterioration was partly ascribed to metal-catalyzed oxidative attack of ether bonds (see references 4,8,10). Coaxial bipolar pacing leads using for inner and outer insulation Pellethane 80A were associated with a high lead failure rate. By 1994, a majority of long-term lead failures reported to the FDA involved a few Pellethane 80A lead models. However, two factors may have contributed to the high failure rates of Pellethane 80A leads. First, treatment with solvents during lead manufacturing adversely affected the integrity of the polymer. Second, lead failures may have partly reflected the mechanical shortcomings of coaxial designs introduced about at the same time as the Pellethane 80A polymer. Coaxial designs tend to produce stiff lead bodies and insulator material between the conductor coils is

susceptible to mechanical degradation. In a preliminary report from the Mayo Clinic (7), failures of ICD leads with coaxial designs appeared to be frequent with both Pellethane 80A (Medtronic 6936 and 6966, n=112) and silicone as the insulator (Medtronic 6934S, Pacesetter 1559, n=34). Contrarily, multilumen silicone leads (Medtronic Sprint, CPI Endotak models, n=214) had relatively low failure rates. From this retrospective analysis, the authors suggested that ICD leads relying on coaxial designs are inherently prone to failure irrespective of the insulating material used (7). Polyurethanes other than Pellethane 80A have been used. Pellethane 2363-55D, a formulation with fewer polyether segments, is stiffer and less prone to stress cracking compared with Pellethane 80A. Although current lead designs make use of 80A and 55D formulations in selected applications, long-term biostability of these applications remain incompletely characterized. Since the degradation of polyether urethanes is partly related to the presence of its ether segments, formulations eliminating these linkages altogether appear desirable. Ideal polyurethane formulations exhibiting both resistance to oxidation and hydrolysis remain to be developed, however (21).

Fluoroethylene Polymers

In addition to silicone rubbers and polyurethanes, fluoroethylene polymers (ethylenetetrafluoroethylene [ETFE] and polytetrafluoroethylene [PTFE, Gor Tex®]) have found increasing application as conductor insulators. Before incorporating conductor cables into silicone rubber, they are covered by layers of extruded ETFE or surrounded by PTFE tubing serving as "redundant" insulation.

In the "coated wire" technique, single nickel-cobalt alloy (MP35N) tubes filled with silver core (drawn filled tubes, DFT) are individually coated with ETFE (4,24,25). Two such wires intended to serve as anodal and cathodal conductors of pacemaker electrodes are placed side-by-side and "parallel-wound" into single "coradial coils". The feasibility of such a design critically depends upon the insulating efficacy and mechanical durability of ETFE wire coating. Since coradial coils serve as stylet pathways, the thin wire coating must be also invulnerable to stylet trauma. In the original Thinline™ coradial bipolar pacing leads (Intermedics/Sulzer), the coradial coils were surrounded by Pellethane 55D to provide redundant insulation and mechanical resistance. The final lead body diameter was 1.7 mm (4.5 F). Preliminary clinical results with the Thinline pacemaker leads have been promising with follow-ups up to 5 years (4,22,23). Guidant is pursuing under the brand name Fineline™ the production of these leads and made both a Pellethane 55D and silicone outer insulations available. Coated wire technology might find an application for the pace/sense electrodes of ICD leads and contribute to the development of thin ICD

leads. However, wire coating as currently used for pacemaker leads might not provide sufficient insulation for the high voltage conductors of ICD leads.

Composite Lead Body Designs

New ICD leads with silicone bodies have incorporated several architectural features to compensate for the drawbacks of silicone lead bodies. First, to reduce the number of lead components and eliminate lead body joints susceptible to delamination and leakage, multilumen lead bodies are made of single pieces of tubing extending from the lead tip to the yoke. Second, air-filled circular or oval channels ("empty" or "crush lumens") are incorporated into lead bodies to increase lead flexibility and unload the silicone elastomer in response to lead compression, bending, and torsion. Third, the silicone rubber of the lead bodies is subjected to various treatments to overcome the unfavorable high coefficient of friction of silicone rubbers. In early designs, high wet friction of silicone prevented low-force sliding of ICD leads past the surfaces of introducers, tunneling tools, vessel walls, and adjacent leads. Forceful manipulation at implantation invited lead damage and vascular (endothelial) trauma. Inert gas plasma treatment (Silacure®, Medtronic) or covalent surface-bonding of crosslinked silicone rubber (Siloxane®, Medtronic) have been used to reduce the adhesiveness of silicone leads. Alternatively, the silicone has been layered or overlaid with lubricious elastomers such as pellethane 55D, Pellethane 80A (Medtronic), or polyvinylpyrrolidone (PVP) (FastPass® and its improved more durable version, SuperPass®, St Jude). No lubricant other than distilled water has been recommended for the implantation of ICD leads. Pellethane overlays have been used to equalize the lead diameter along the entire lead, "isodiametric designs" aimed at facilitating lead implantation and extraction.

Drug Elution

One technology likely to gain in importance is the adsorption or incorporation of drugs onto or into lead elastomers. Elutable drugs include antiinflammatory/antiproliferative/immunosuppressant agents (steroids, rapamycin), antithrombotic agents (heparin), and antibiotics. Rapamycin, a new drug with immunosuppressant and antiproliferative properties, has been successfully used to prevent coronary stent restenosis, but to our knowledge has not been tested for the suppression of proliferative responses to ICD lead bodies and electrodes. Drug elution (steroid) has been already extensively applied to reduce the inflammatory response to tip electrodes (see below). Antibiotics might be also adsorbed to the surface of generators

(re-) implanted when special infection risk factors prevail (see chapter "Implantation", topical prophylactic antibiotics).

Precautions Against Insulator Damage

In addition to architectural designs aimed at protecting silicone lead bodies such as mechanically resistant lubricious overlays or empty channels for stress relief, the integrity of silicone leads can be preserved by careful lead manipulation at implantation. Different lead handling provides a potential explanation for marked differences in lead failure rates reported by different investigators. Because silicone rubbers have a low tear strength and crush resistance, it is important to handle silicone leads as gently as possible. This includes preference of cephalic over (medial) subclavian venous access (24,25), avoidance of stretching the leads during tunneling maneuvers (25), and avoidance of placing constricting sutures around the suture sleeves of the leads. No sutures should be placed directly around the leads (see chapter "Implantation"). Pectoral implants associated with silicone lead failures have been related to large generators (>195 g, >115 ml) and compressive forces within undersized pockets in combination with redundantly long leads (5,18,19,24,25,26). Such implant conditions invite lead abrasion and frictional damage. Implanters should remember that silicone insulator failures have been associated with specific avoidable implantation risk factors.

CONDUCTORS

An important advance in conductor design was the use of multifilar cables shaped into coils. The lumen of these coils serves as a pathway for stylets that provide essential guidance for lead implantation. The stainless steel conductors used in original lead designs were replaced by more fatigue- and corrosion-resistant nickel cobalt alloys such as MP35N. Typical multifilar conductor cables are composed of several MP35N wires. Individual wires consist of drawn braided strands (DBS) or drawn filled tubes (DFT) of MP35N incorporating a low resistance core such as silver. These "composite wires" unite desirable mechanical and electrical properties (Table 1).

ELECTRODES

Pace/Sense Electrodes

Over the last 30 years there has been a trend from large (surface area ~ 100 mm²) to pinpoint-sized ("nanotip") pacing electrodes (1.0 mm²) that increase the pacing impedance from about 100 to 1000 ohms. Increasing pacing impedance lowers current drain, very important for ICDs subserving both defibrillation and multisite pacing. However, the benefit derived from

decreasing electrode size has theoretical and experimental limits and reductions below a 1.6 mm^2 surface area may not substantially diminish energy thresholds as long as pulse durations are kept at 0.5 ms (27). Small electrodes were initially felt to be unsafe because of their perceived sensitivity to microdisplacement and proneness to perforate (28). However, initial experience suggested that small steroid-eluting electrodes were relatively safe and helped to reduce energy consumption as postulated (29-32). In a study of Medtronic leads with steroid eluting microporous platinum tip electrodes, 1.2 mm^2 high-impedance electrode leads ($n=290$; ventricular 5034 and atrial 5534 Capsure Z-models) compared with 5.8 mm^2 electrode leads ($n=319$; ventricular 5024 and atrial 5524 Capsure SP models) reduced pulse energy consumption in both atrial and ventricular positions by about 47-55% without adversely affecting stimulation threshold and sensing (30). Complication rates did not differ between high impedance and control electrodes (30). In another similar comparison study of Capsure Z (low impedance) and Capsure SP (control) leads involving 188 patients, Moracchini et al (31) reported similar results. These and other studies (for refs see 29-32) suggest that leads with high impedance at the electrode/tissue interface may appreciably reduce current drain from pacing with dedicated bipolar electrode systems. However, using newly developed high impedance electrodes there is a persistent concern about early loss of capture (8,28).

Electrode composition is critical to the long-term performance of electrodes. Stainless steel, used in early designs (2), is unacceptable because "oxidation-resistant" iron alloys do corrode with consequent inflammation and fibro-proliferative response at the electrode tissue interface. Platinum, although relatively inert, undergoes anodal oxidation. Platinum containing iridium increases its mechanical strength and is appropriate in cathodal position. Highly purified vitreous (pyrolytic) carbons with oxidatively texturized ("activated") surface have been used as a cathode material. Titanium alloys, coated titanium, and titanium nitride are suitable for both anodes and cathodes. The relative merits of the different materials in current use are uncertain. Most clinical lead studies may not have the required statistical power to distinguish by appropriate statistical methods (Kaplan-Meier and Cox analyses) independent risk factors of electrode material, electrode design, surface structure, and steroid elution (29-32).

Lead impedance (resistance to nonsteady (alternating) electric current), in addition to its dependence on electrode geometry (surface area [27]), is importantly determined by several factors: impedance of the lead connector, impedance of the lead conductor, lead length, polarization of the electrode, and impedance of the electrode-tissue interface. High conductor impedance results in wasteful heat dissipation within the lead body. Thus, although

high pacing impedance reduces current drain, this desirable effect should be achieved at the electrode-tissue interface, not as resistance in the lead conductor. In the drawn tube technology described above, the inclusion of a silver core reduces the ohmic resistance of the MP35N tubing by about 90%.

Factors that received considerable investigative attention are electrode polarization and the biologically modulated electrode-tissue interface, since these factors play a pivotal role in the sensing and stimulation performance of an electrode in a biological milieu. The transfer of electric energy from a metal, in which current depends on electron flow, to tissue, in which current depends upon ion movement, involves an electrochemical reaction known as polarization. Ions of opposite charge align on the positive and negative electrode surfaces, hampering the transfer of charge for effective pacing and sensing. Electrochemical polarization increases with decreasing electrode surface area and increases with increasing stimulation current. It depends upon many factors including electrode alloy composition, electrode surface structure, and time since implantation. Polarization effects can account for a substantial percentage of the total pacing impedance with values of up to 70% using small smooth-surface electrodes. The introduction of porous electrode surfaces in the late 1970ies allowed increases in electrode surface area without concomitant increases in electrode size, a maneuver that minimizes polarization effects. Numerous strategies were applied to achieve microporous increases in wettable surface areas including electroplating of platinum powder, coating with platinum iridium or titanium nitride, thermally bonding iridium oxide onto titanium (IroxTM Intermedics), laser drilling, and others. These various treatments may decrease electrode polarization by as much as 90%. Experimentally, the major determinant of chronic pacing threshold within clinically useful electrode dimensions is not so much the geometric surface area or shape of the electrodes, but their surface structure. It is crucially important to reduce polarization since it limits or eliminates the benefits derived from high impedance electrodes (8,10,29-32). In pacemakers designed to monitor automatically pacing threshold (automated capture control), polarization effects may hinder the detection of local myocardial depolarization, sign of capture, and defeat algorithms of automated detection (e.g., Pacesetter AutoCaptureTM) (10,33). Textured metallic surfaces, in addition to limiting polarization, facilitate tissue ingrowth necessary for stable electrode anchoring.

The early rise in stimulation threshold typically observed during the first few weeks after implantation are ascribed to an inflammatory response to the implanted foreign body. Influence of systemic glucocorticoid on pacing thresholds supports this concept. Still, the determinants of the transient rise in pacing threshold after implantation are incompletely understood. In early

clinical trials involving small patient groups (9-18 patients) and follow-ups of 6-24 months, inclusion of a steroid-elution system at the lead tip reduced the early rise in stimulation threshold compared with nonsteroid controls (34-36). Both atrial and ventricular leads exhibited beneficial effects from steroid elution (8). These trials and subsequent studies also showed that low stimulation thresholds and energy sparing effects were maintained for up to 5 years (37). However, effects of steroid elution may depend upon the electrode type and anchoring mechanism used. In one recent study, patients randomized to a microporous titanium nitride tip electrode with (1450 T, n=51 patients) or without (1451 T, n=45 patients) dexamethasone added to the polymer coating the cathode (surface area 3.2 mm^2) exhibited *no* transient rise in voltage threshold in *either* group (38). The authors concluded that the tip design as such, irrespective of steroid additive, prevented energy-consuming increases in voltage threshold (38). The suggestion that some microporous electrodes may exhibit a "tunnel-effect" eliminating the early transient threshold rise will require further evaluation. Most manufacturers currently producing defibrillator leads make steroid-eluting models available. To our knowledge, no prospective double blind study of an ICD electrode with placebo (inactive steroid) or steroid elution has been reported.

Pace/sense electrodes of defibrillator leads resemble those of pacemakers. The tip electrode surface areas range from 1.6 to 8.5 mm^2 . The electrode material (both for cathodal tip and anodal ring pace/sense electrodes) is often platinum iridium with titanium nitride coating, a microporous conductive ceramic.

Defibrillation Electrodes

There is currently a relative uniformity of high voltage coil sizes among different manufacturers. Ventricular (distal) shock electrodes are usually about 50-57 mm long with a diameter of 2.7-3.1 mm and a surface area of 350 - 585 mm^2 . In dual shock leads, proximal and distal coils have the same diameter, but proximal coils are 44-60% longer (72-80 mm) and have therefore a larger surface area (560 - 670 mm^2). Tying the conductor to each end of the defibrillation coils ensures during discharge uniform current density along the entire coil length. There is some experimental evidence that the surface area of ventricular defibrillation electrodes is an important determinant of defibrillation efficiency (39-41). However, defibrillation electrodes under current development use thin defibrillation coils (1.8 mm or F 6) without apparent decreases in defibrillation efficiency. Thinner and therefore more flexible defibrillation coils may conform more easily to the right ventricular cavity and thereby improve defibrillatory electric fields. High voltage coils are usually made of platinum/iridium alloys. There is little clinical information available on the effects of high voltage coils with

increased surface areas produced by microporous coatings. Contrarily, there is experimental evidence that defibrillation efficacy is insensitive to the variation of active can size (from 20 to 80 ml) in the presence of an invariant right ventricular coil (42). This result is consistent with the relative insensitivity of the defibrillation threshold to the positioning of active cans on the chest (see chapter "Implantation").

Integration of High and Low Voltage Electrodes

The development of leads for both defibrillation and pace/sensing has lead to two electrode designs (Table 1) (19). In the "dedicated" or "true" bipolar system, a typical distal bipolar pace/sense electrode is incorporated into a lead with a single or dual high voltage coil. For single high voltage coil systems to operate, a second independent lead with high voltage coil and/or an extrathoracic electrode ("active can", "lead array" [Endotak SQ Arrays], subcutaneous patch) is necessary. In the so-called "integrated" approach, there is only one distal dedicated pace/sense electrode (tip cathode). The pacing anode is provided by a promiscuous distal coil serving also as a ventricular high voltage electrode. Such leads may have additionally a second proximal high voltage electrode ("dual coil" electrodes pioneered by Guidant/CPI under the name Endotak™). Dual coil electrodes, conceived before the advent of active cans, can singly provide ventricular pacing, sensing, and defibrillation, although high defibrillation thresholds achieved by these leads may require additional electrodes. Dual coil electrodes have certain drawbacks. The necessary multilumen constructions has thus far resulted in thick leads (diameter ≥ 2.7 mm) and design complexity makes the leads vulnerable to manufacturing and post-implantation failures (see above, "Conductor"). With a small distance (≤ 8 mm) between the pacing cathode and distal defibrillation coil, one may observe post-shock impairment in pacing and sensing, manifested as an elevated pacing threshold (43,44) and a failure to redetect ventricular fibrillation after an unsuccessful shock (45,46). Contrarily, increasing the spacing between these electrodes to ≥ 12 mm can minimize post-shock impairment of low voltage electrode performance, but may limit defibrillation efficiency because of increasing remoteness of the defibrillation coil from the ventricular (apical) myocardium. The optimum spacing between pacing and defibrillation electrodes in integrated configurations remains controversial and varies among different ICD lead models between 6-24 mm. However, differences in performance between dedicated and integrated leads in current use may not be as marked as sometimes insinuated. Differences in post-shock low voltage lead dysfunction between integrated (interelectrode spacing ≥ 12 mm) and dedicated pacing electrodes were absent in some studies (45,46). Based on observations in 20 patients failing to demonstrate differences between

integrated and dedicated pacing electrodes, Welch et al. (45) recommended to set postshock pacing at least 4x threshold *regardless* of lead design.

Recently, quadripolar ICD electrodes with dual high voltage coils as well as dedicated pace/sense electrodes have been developed (e.g., Sprint Quattro 6944 and 6947, Medtronic; Vectra 1570 and 1580, St. Jude). The Sprint quadripolar ICD lead has a close spacing (8 mm) between the pace/sense tip cathode and anode ring, which should provide optimum sensing and minimize far-field interference (see chapter "Environmental Interference"). Concomitantly, the right ventricular shock electrode is still kept close to the lead tip (tip to coil spacing 12 mm) to insure effective defibrillation. If quadripolar leads can avoid increased failure rates, they might lead to the abandonment of integrated designs. However, compared with complex multilumen leads, simpler but thinner lead designs remain an attractive option. Truly randomized controlled long-term studies would be needed to compare these opposite philosophies of lead design.

FIXATION

In the late 1970ies, leads with small tines positioned behind the tip electrode achieved for the first time highly reliable lead tip fixation and revolutionized lead implantation. Subsequently, many other systems of lead fixation were proposed and tested. Fixation mechanisms, pace/sense electrode design, and steroid elution systems are lead characteristics that interdependently determine pace/sense performance, fixation, and extractability. "Passive" fixation mechanisms consist of rubbery (silicone) tines, fins, cones, or wings radiating from the lead end like the ribs of an umbrella. The lead tips are pushed perpendicularly against the endocardial surface with the aim to hook their radial protrusions to endocardial trabeculations. "Active" fixation usually makes use of metallic screws or helixes topping the lead tip and requiring both an axial and rotational force for endocardial insertion. Nonretractable screws are fixed to the lead tip and are now usually covered with a blood-soluble solid such as mannitol or polyethylene glycol (solving times ca. 4 min) to facilitate atraumatic lead implantation and avoid tricuspid entanglement. Rotation of fixed screws requires axial torsion of the lead body. In retractable screw designs, initial retraction of the screw from the lead tip facilitates atraumatic advancement and positioning of the lead. An advantage of retractable leads is their active "mapping collars". Positioned at the lead tip, these collars can establish temporary myocardial contact for the selection of optimal insertion sites without the need to deploy the screw. Once a site is selected under combined electrophysiologic and fluoroscopic control, the screws are extended into the myocardium. The Endotak™ leads (Guidant) use a flat-tip stylet accomplishing a screwdriver function to rotate the helix with a one-to-one torque transfer. In other designs such as those used by

Ventritex/St. Jude and Medtronic, torque for the screw is transmitted via the pace/sense (IS-1) connector pin and conductor. Screw fixation is largely independent of trabecular formations and is more traumatic than passive fixation systems. However, steroid elution systems and microporous electrode surfaces may counterbalance the adverse effects of screw trauma and minimize early rises in pacing threshold. Postulated advantages of active fixation are atraumatic lead advancement, increased ventricular and particularly atrial placement options, and facilitated lead extractability compared with passive anchoring. The helix of retractable pacing leads may be either electrically active or passive. The retractable helixes of most Medtronic, Ventritex/St. Jude, and Guidant defibrillator leads are electrically active. Randomized, appropriately powered trials of ICD leads to demonstrate superiority of one fixation mechanism system over another have to our knowledge not been performed. We believe that in experienced hands, lead tip dislodgment rates below 2% (47) and perforation rates below 1% (47-49) should be readily achievable in consecutive patients irrespective of lead models used. Long-term defibrillator lead failure rates tabulated in some reviews varied in different studies between 2 and 28% (9), a disconcerting range precluding valid meta-analyses. As alluded to under "Precautions Against Insulator Damage", the variability in the rates of implantation complications may depend upon operator-dependent factors including lead handling (50). Therefore, strikingly variable complication rates with specific lead models without information about participating implanters are difficult to interpret.

CORONARY VENOUS LEADS (LEFT VENTRICULAR PACING LEADS)

New dual chamber ICDs have incorporated advanced pacemaker technology. Of particular interest are atrioventricular pacing strategies for the "resynchronization" of ventricular contraction. Limited evidence from cross-over trials suggests that biventricular pacing may improve heart failure in patients with intraventricular conduction delay (51). Importantly, several recent reports have suggested that biventricular pacing may reduce long-term risk of ventricular tachyarrhythmias (52-54). Because of the current interest in the field and because multichamber pacing in heart failure always requires defibrillator backup, equipment specially developed to facilitate this type of therapy is discussed here. Major manufacturers have all developed coronary catheterization systems that are currently under clinical evaluation (Easytrak (Guidant), Aescula (St. Jude), Attain (Medtronic)).

"Over the wire" strategies as developed for coronary angioplasty have been adapted to coronary vein lead placement for left ventricular pacing via a transvenous route (e.g., Easytrak, Guidant; Attain-OTW, Medtronic). The

Easytrak system is a transvenous, coronary venous, steroid eluting, unipolar pace/sense lead for left ventricular stimulation (55). The lead is delivered through an 8 F guiding catheter with torquability to facilitate coronary sinus access. The catheter tip has a soft tip to prevent atrial and coronary sinus trauma. The 6 F lead has an open lumen conductor coil designed to accommodate a standard 0.014 inch PTCA guidewire. The pace/sense ring electrode is positioned proximal to a soft silicone tip to prevent chronic vein erosion and perforation. The electrode has a steroid eluting collar and two silicone tines for endovenous anchoring. The distal silicone lead body is reinforced with a lubricious polyurethane sleeve to protect it from friction against the right ventricular lead.

Coronary sinus catheterization with over the wire (OTW) techniques should be performed with the guiding catheter containing a 6 F deflectable tip mapping catheter (or a guidewire) for guidance. After stabilization of the guiding catheter deep in the coronary sinus and withdrawal of the mapping catheter, the absence of coronary sinus trauma is evaluated venographically by delivery of small amounts of contrast (1-5 ml) into the coronary sinus. If persistent staining to suggest coronary sinus dissection is demonstrated, the procedure should be terminated and possibly attempted again 2-4 weeks later. If no coronary sinus staining is demonstrable, the variable coronary venous anatomy (56) can be visualized injecting a slightly larger amount of dye (10-20 ml). To avoid coronary sinus trauma, it is recommended to perform venography whenever possible without transient coronary venous occlusion achieved by advancing a balloon catheter through the guiding catheter. The lead with guidewire is then advanced through the guiding catheter and positioned in the great cardiac vein. Guided by venographic information, the guidewire is further advanced to a desirable venous location. The lead is then advanced over the wire until resistance suggests venous wedging of the lead tip. The guidewire is removed and replaced by a finishing wire used to stabilize the lead during withdrawal of the guiding catheter. For optimal therapeutic benefit, a lateral left ventricular electrode position midway between apex and base has been recommended (51-55). Because coronary vein catheterization for biventricular pacing is occasionally a lengthy procedure (4-5 hours), antibiotic prophylaxis with intraprocedural repeat dosing should be used (see chapter "Implantation").

Lead systems developed for coronary vein catheterization remain investigational tools. Catheters for bipolar coronary venous pacing are under development and should soon become available for clinical testing. The feasibility and safety of the transvenous extraction of different coronary sinus leads remain to be evaluated.

REGISTRY

A North American pacemaker and ICD lead registry, similar in concept to the European STIMARC registry, has been initiated at the Minneapolis Heart Institute under the direction of Robert Hauser (57). Registries free of conflict of interest are important and their support by practicing electrophysiologists is strongly encouraged (9,57-59).

CONCLUSIONS

Significant advances in lead technology have been achieved in recent years. Defibrillation leads incorporate modern bipolar pace/sense electrode designs including high impedance, microporous electrode surfaces, steroid elution, and low polarization (Table 1). Thinner ICD leads partly or entirely substituting silicone with new insulator materials and tetrapolar leads with dual coil and dedicated pacing electrodes have been developed. Publications on defibrillator lead failures are often based on retrospective analyses of small series. Studies of long-term lead complications have shown strikingly variable results in these series. Some large retrospective surveys suggest that defibrillator leads can be implanted with dislodgment rates below 2% and perforation rates below 1%. Multicenter studies have generally failed to discern between operator-dependent and operator-independent factors of acute and long-term lead failure rates. Because of the paucity of adequately powered randomized studies in the field, conclusions about the superiority of specific designs should be made cautiously.

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X. Related Proceedings Appendix

There are no related proceedings at this time.